PUBLISHED WEEKLY

PRICE TWO SHILLINGS AND SIXPENCE

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—41ST YEAR SYDNEY, SATURDAY, SEPTEMBER 18, 1954 No. 12

Registered at the G.P.O., Sydney, for transmission by post as a newspaper.

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NASAL CARRIAGE OF STAPHYLOCOCCUS AUREUS IN THE GENERAL POPULATION AND ITS RELATIONSHIP TO HOSPITALIZATION AND TO PENICILLIN THERAPY.

By PHYLLIS M. ROUNTREE, BARBARA M. FREEMAN and R. G. H. BARBOUR,

Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Sydney.

DURING the past six years there has accumulated world-wide evidence of an increased incidence of penicillin-resistant pathogenic staphylococci isolated from patients in hospital. As a result of this increase penicillin is no longer recommended for the therapy of staphylococcal infections arising in hospitals. In those hospitals where the incidence of strains resistant to other antibiotics has been investigated, similar increases in the incidence of such strains have been demonstrated following the introduction of the newer antibiotics. For example, in the Walter Reed Army Hospital in Washington (Roerig *et alii*, 1953) 72·5% of strains isolated from wounds were resistant to penicillin, streptomycin, chlortetracycline and oxytetracycline. In all places where phage typing has been done it has been shown that only a few of the many possible phage patterns are implicated in these nosocomial infections, and that, with few exceptions, the resistant strains have belonged to one particular broad group of *Staphylococcus aureus*—namely, Group III (Williams, Rippon and Dowsett, 1953; Rountree, 1953).

Less information, however, is available as to the present incidence of penicillin-resistant strains in the general community. From the point of view of the general practitioner it is clearly important that this information, which will also be of value in ecological studies, should be available. Figures obtained from patients attending hospital out-patient or casualty departments may not necessarily reflect the true incidence in the community at large, since such patients may already have been in contact with the hospital environment. In this hospital, of 457 strains isolated from casualty patients and out-patients between February, 1952, and March, 1954, 176 (38·5%) were penicillin-resistant. It is likely that many of these strains were from people with long-standing infections who had received penicillin therapy, or from people already acquainted with the hospital and liable to return to it as casualty patients or out-patients.

Summers (1952) examined strains from 568 out-patients attending the Radcliffe Infirmary at Oxford and showed that 24% were penicillin-resistant. If, however, allowance was made for previous contact with the hospital, then the incidence was only 6% in "closed" lesions (septic fingers, hands, toes *et cetera*) occurring in 211 patients attending the casualty department and with infrequent or

no hospital contact. Similarly, Eriksen (1952) in Denmark, between October, 1949, and February, 1952, examined 293 strains from lesions in out-patients in the surgical clinic of the Rigs Hospital in Copenhagen, and found 5·1% to be penicillin-resistant. These patients had not been treated with penicillin, whereas the incidence in 87 patients treated with penicillin was 21·8%.

If it is accepted that the anterior nares are the reservoir of *Staph. aureus*, then nasal carrier rates should be a reliable index of the incidence of antibiotic-resistant staphylococci in any given sample of a population. Here again there is not a great deal of information. In Norway, Vogelsang (1951) examined, in 1949, 1304 strains isolated from the nose and throat of 1000 fourteen and fifteen year old schoolboys, and found 3·9% to be resistant to penicillin, not being inhibited by 5·7 units per millilitre. A further 1·5% were relatively resistant, 0·17 to 5·7 units per millilitre inhibiting growth. Martin and Whitehead (1949) studied 83 strains isolated from various sites in a group of 50 male adult medical students and laboratory workers in London; 31 of these people were carriers on one or more sites, and six (19·4%) were carrying penicillin-resistant strains. This fairly high incidence may possibly have been due to the fact that at least a proportion of these people were in contact with a hospital environment.

More recently, Oswald, Reedy, Randell and Welch (1953) examined 119 coagulase-positive strains isolated from 213 young adult males at physical examination for entrance into the United States Army. The sites from which these strains were obtained is not recorded in their paper, but presumably it was from the skin or respiratory tract. Of the strains, 16 (13·4%) were moderately resistant to penicillin, being inhibited by 1 to 10 microgrammes per millilitre, and 16 (13·4%) were highly resistant, being inhibited only by 10 to 100 microgrammes per millilitre.

In Sydney, on two occasions, nasal carrier rates have been determined in blood donors at the Red Cross Blood Transfusion Service. In 1949 (Rountree and Thomson) eight of 90 carriers found among 200 donors yielded penicillin-resistant strains. In 1951 (Rountree) seven of 95 carriers found in a sample of 200 donors were carrying penicillin-resistant strains. In the two years there had therefore been no increased incidence.

In March and April of this year a further survey of blood donors was made, with the particular object of determining if there had been any significant increase in the incidence of antibiotic-resistant strains in the intervening three years. In the present survey each donor was also asked whether he or she had received penicillin in the past five years or had been in hospital during that period.

All strains of staphylococci isolated were examined for coagulase production. Sensitivity to penicillin, streptomycin, chloramphenicol, oxytetracycline and chlortetracycline was determined on the coagulase-positive strains by the plate disk method, and these strains were also phage typed.

Nasal Carrier Rates in Blood Donors.

The nasal carrier rates found are summarized in Table I. Of the 200 people from whom swabs were taken, 98 (49%) were carrying *Staph. aureus*—an incidence similar to those previously found in blood donors. Thirteen (13·4%) of these carriers were carrying penicillin-resistant strains. Comparison of this carrier rate of resistant strains with that obtained in 1951 shows an increase of 6%. Statistical analysis gives the following findings: $\chi^2 = 1{\cdot}80$, $P < 0{\cdot}2 > 0{\cdot}1$. The difference cannot therefore be regarded as statistically significant. Nevertheless it does indicate a not unimportant trend.

No strains resistant to streptomycin or chloramphenicol were found, but one donor was carrying a strain resistant to penicillin, oxytetracycline and chlortetracycline. This donor had recently been in hospital, where he had received "Aureomycin" therapy.

Of the 13 penicillin-resistant strains, 12 belonged to Group III and one was not typable with any available phages. The frequency distribution of the penicillin-sensitive strains in the various phage groups was similar to that found in strains isolated from normal persons on previous occasions (Rountree, 1953).

Relationship of Nasal Carriage to Penicillin Therapy and to Hospitalization.

Under the circumstances of the survey it was not possible to determine the quantity or duration of penicillin therapy. Of the 200 people questioned, four were uncertain as to whether they had received penicillin; 95 (47·5%) of the remainder stated that they had received some form of penicillin therapy. Five had used penicillin lozenges, one eye drops, and another penicillin cream. Eighty-eight of 200 people had therefore received penicillin parenterally. Forty-nine (51·6%) of those who had had penicillin were nasal carriers, and eight of the 13 penicillin-resistant strains isolated came from these carriers.

Forty-seven of the 200 donors had been in hospital, six having been in maternity hospitals. This corresponds to a rate of 47 per 1000 per year. Admissions to hospitals in New South Wales for the year ending June, 1953, and excluding tuberculosis hospitals, mental hospitals, and children's hospitals and homes for the aged, were 379,628, a rate of approximately 130 per 1000. This sample of blood donors therefore contained a smaller proportion of people who had experienced hospital care than would have been found in a completely random sample of the community. Of the 47 people who had been in hospital, 30 (63·8%) stated that they had received penicillin and one was not certain. Of the 153 people who had not been in hospital, 71 (46·4%) had received penicillin and three were not sure. As was expected, there was a high incidence of penicillin therapy among the people who had been in hospital; but the extent of penicillin therapy outside hospitals was more surprising.

The nasal carrier rate among donors who had been in hospital was 57·5%, and among those who had not been in hospital, 46·4%. This difference is not statistically significant, but there is a trend towards higher carrier rates in the persons who had been in hospital. Four of the 27 carriers who had been in hospital were carrying penicillin-resistant strains.

When the effects of penicillin therapy and hospitalization were considered together in relationship to nasal carriage,

TABLE I.

Nasal Carrier Rates of Staphylococcus aureus *in Blood Donors.*

Category.	Nasal Carriers of *Staphylococcus aureus*.						
	Number.	Penicillin-Sensitive Strains.		Penicillin-Resistant Strains.		Total Carriers.	
		Number.	Percentage.	Number.	Percentage.	Number.	Percentage.
Blood donors	200	85	86·6	13	13·4	98	49·0
In hospital	47	23	85·2	4	14·8	27	57·5
Not in hospital	153	62	87·3	9	12·7	71	46·4
Received penicillin	95	41	83·7	8	16·3	49	51·6
No penicillin	101	42	89·3	5	10·7	47	46·5
Hospital and/or penicillin	112	50	83·3	10	16·7	60	53·6
No hospital or penicillin	84	34	91·9	3	8·1	37	44·0

it was found that only three of the donors who had had no experience of either hospitals or penicillin therapy were carrying antibiotic-resistant staphylococci. The remaining 10 carriers had either been in hospital or had received penicillin, or both. The figures obtained are too small to be statistically significant, but they do suggest an association of penicillin-resistant strains with penicillin therapy and/or hospitalization.

Summarizing the results, one may say that they indicate a trend towards an increasing incidence of penicillin-resistant staphylococci in this sample of the population of Sydney. The proportion of people who had been in hospital suggests that the sample was not altogether an unbiased one and emphasizes the difficulty of obtaining a completely random sample of any given population. However, the people examined did comprise a broad sample with regard to age and occupation.

Among those who had not been in hospital, the fairly high proportion whose nasal carriage of penicillin-resistant staphylococci was associated with a previous history of penicillin therapy indicates that conversion to resistance during penicillin therapy should be considered as a probable factor in the appearance of these resistant strains in the general community.

Observations on the Relationship of Hospitalization to the Nasal Carriage of Staphylococcus Aureus.

Hospitalization exposes the patient to an environment more or less heavily contaminated with staphylococci and therefore to the risk of staphylococcal cross-infection, particularly of burnt or wounded skin surfaces. It follows that one may also expect hospital strains of staphylococci to be implanted on the patient's nasal mucosa. Rountree and Barbour (1951) showed that the exposure of trainee nurses to the hospital environment did result in many of them becoming nasal carriers of the antibiotic-resistant strains characteristic of the hospital at the time of their entry in the wards. However, there is not a great deal of information on the effect of hospitalization on nasal carrier rates in patients. Miles, Williams and Clayton-Cooper (1944), using a weekly swab as the index of nasal carriage in patients in a Birmingham hospital, showed that there was an over-all 5·1% increase in the nasal carrier rate after a stay in hospital. More recently, Lepper *et alii* (1953) in Chicago examined 533 patients, 25·1% of whom were nasal carriers on their admission to hospital. Of the non-carriers on admission to hospital, 28·1% became carriers during their stay in hospital. These workers also showed that patients who had received no antibiotic therapy while in hospital had an increased incidence of antibiotic-resistant strains, evidently due to their acquisition of hospital strains.

In 1950 and 1951 some observations were made in this hospital on the changes in nasal staphylococci of patients in surgical wards. Two groups of patients were studied. The first group was admitted to the male and female ophthalmological wards and had nasal swabs taken on the days of admission to and of discharge from hospital. The second group was admitted to a male and female general surgical ward, and swabs were taken on admission and thereafter at weekly intervals. The first group therefore gave information only on the nasal flora on admission and discharge, while the second group gave additional information on the time that elapsed before the acquisition of a new strain.

Table II shows that 153 patients were examined. Their carrier rate on admission to hospital was 34%, which is lower than that found in other samples of the general population. The mean ages of the two groups of patients were fifty-nine and forty-four years respectively, and it is possible that relatively greater ages may be correlated with lower carrier rates.

The carrier rate rose to 40·5% on discharge from hospital. In the ophthalmological wards ten patients acquired new strains before their discharge, eight having been non-carriers on admission to hospital, and in two a strain appeared that differed from that carried on admission to hospital. Three carriers on admission to hospital became non-carriers. In the general surgical wards 21 of 78 patients acquired pathogenic staphylococci in their noses while in hospital, and 17 of these people were carrying the acquired strains when they were discharged. The other four patients were "temporary" carriers only, the organisms being isolated at one or two weekly swabbings, but disappearing before the patients left hospital. In four cases a hospital strain replaced the strain carried on admission to hospital. In the remainder the strains were implanted in non-carriers.

TABLE II.

Nasal Carrier Rates of Staphylococcus aureus *in Hospital Patients.*

Ward.	Number of Patients.	Mean Age. (Years.)	Nasal Carriers of *Staphylococcus aureus*.			
			On Admission.	On Discharge.	Acquired Strains.	Lost Strains.
A4	75	59	25	30	10	3
V3	78	44	27	32	17	8
Total	153	—	52 (34·0%)	62 (40·5%)	27 (17·6%)	11

At the period during which these observations were made, the predominant staphylococci responsible for cross-infection in the hospital were penicillin-resistant and often streptomycin-resistant strains belonging to phage patterns 31B or 47/31B. Eighteen of the 31 strains acquired were of this type.

Table III, which includes the four "temporary" carriers, shows that the majority (17 of 21) of patients who acquired new strains did so before the end of the first or second week's stay in hospital. The mean length of time during which the persistent non-carriers were observed was sixteen days, so that there was adequate time for these people to have become carriers.

TABLE III.

Length of Stay in Hospital when New Strain of Staphylococcus aureus *Detected.*

Days of Stay in Hospital.	Number of Patients.	
7	11	21
14	6	
21	1	
28	1	
35	2	

Mean stay in hospital: 13·3 days.

This survey, limited though it was, therefore showed that hospitalization resulted in the acquisition by the patients of hospital strains of *Staph. aureus*. The length of time for which these people continued to carry the antibiotic-resistant staphylococci in their noses after discharge from hospital is, however, unknown. So far as we are aware, the only specific information on this subject is provided by a recent study carried out in Chicago by Dowling, Lepper and Jackson (1953). These workers examined patients and their household contacts on the patients' discharge from hospital and thereafter at weekly intervals. They found a higher carrier rate in the patients on discharge than in their household contacts; but at the end of four weeks after discharge the patients' carrier rates had fallen to the same level as the rest of the household. In their paper, although a high incidence (25%) of penicillin-resistant staphylococci is reported in the household contacts on initial examination of swabs, no distinction is made between coagulase-positive and coagulase-negative staphylococci, and it is therefore not possible to compare this incidence with those reported for *Staph. aureus* by other investigators. However, bacteriophage

typing, presumably of coagulase-positive strains, did show that in seven of the 54 households investigated the strain brought home from the hospital was transferred to another member of the household. This method of acquiring antibiotic-resistant staphylococci must evidently be taken into account when the spread of these strains in the general population is being considered.

Conclusions.

The results described in this paper should be regarded as an interim report on the ecological changes taking place in our staphylococcal flora. The change of hospital staphylococci from penicillin sensitivity to resistance has occurred with quite startling rapidity, but the great selection pressures that exist in hospitals should not be expected to operate to the same extent in the general population. Nevertheless, our present investigations and those of other workers do indicate a gradually increasing incidence of penicillin-resistant staphylococci outside hospitals. Acquisition of these strains by patients while in hospitals, their transfer to other members of the community and the selection of resistant mutants during penicillin therapy must all be considered as contributing to this increasing incidence.

From the figures obtained from the blood donors one would anticipate that at present, on an average, penicillin therapy would be effective in six out of seven people presenting themselves to general practitioners for treatment of acute staphylococcal infection.

The widespread use of penicillin revealed by the survey was perhaps not altogether surprising when one considers the enthusiasm with which it is prescribed, in many cases on slender bacteriological grounds. Timely warnings continue to be uttered on the consequences of over-zealous exhibition of antibiotics, and it would seem that these must be reemphasized. It would be alarmist, and indeed without factual basis, to state that there is as yet a substantial conversion to antibiotic resistance of our staphylococcal flora outside hospitals. Clearly, however, a trend towards increasing resistance is apparent and should be carefully watched.

Summary.

A survey was made in March and April, 1954, of the nasal carrier rates of *Staph. aureus* in a series of 200 blood donors in Sydney.

The nasal carrier rate was 49%; 13·4% of these carriers were carrying penicillin-resistant strains, an increase of 6% on the incidence found in 1951. There appeared to be an association between nasal carriage of resistant strains and a past history of penicillin therapy and/or hospitalization.

Investigation of the nasal flora of 153 hospital patients showed that 17·6% had acquired new strains of staphylococci in their noses by the time they left hospital.

Acknowledgements

This work was supported by a grant from the National Health and Medical Research Council, Commonwealth of Australia. Our grateful thanks are due to the Director of the New South Wales Branch of the Red Cross Blood Transfusion Service for his cooperation in allowing us access to the donors. We are indebted to the Secretary of the New South Wales Hospitals Commission for the information on admissions to hospitals.

References.

DOWLING, H. F., LEPPER, M. H., and JACKSON, G. G. (1953), "Observations on the Epidemiological Spread of Antibiotic Resistant Staphylococci, with Measurements of the Changes in Sensitivity to Penicillin and Aureomycin", *Am. J. Pub. Health*, 43: 860.

ERIKSEN, K. R. (1952), *"Nosocomiel Infektion med Stafylokokker Resistente overfor Penicillin og andre Antibiotica"*, *Ugesk. f. laeger*, 114: 1607.

LEPPER, M. H., DOWLING, H. F., JACKSON, G. G., and HIRSCH, M. M. (1953), "Epidemiology of Penicillin- and Aureomycin-Resistant Staphylococci in a Hospital Population", *Arch. Int. Med.*, 92: 40.

MARTIN, T. D. M., and WHITEHEAD, J. E. M. (1949), "Carriage of Penicillin Resistant Staphylococcus Pyogenes in Healthy Adults", *Brit. M. J.*, 1: 173.

MILES, A. A., WILLIAMS, R. E. O., and CLAYTON-COOPER, B. (1944), "The Carriage of Staphylococcus (Pyogenes) Aureus in Man and its Relation to Wound Infection", *J. Path. & Bact.*, 56: 513.

OSWALD, E. J., REEDY, R. A., RANDALL, W. A., and WELCH, H. (1953), "Penicillin Resistance Encountered in Staphylococci Isolated from Selected Groups", "Antibiotics Annual" Medical Encyclopedia Inc., New York: 318.

ROBRIG, R. N., METZGER, J. F., FUSILLO, M. H., and ERNST, K. F. (1953), "Phage Typing of Antibiotic-Resistant Staphylococci. II. Phage Typing of Organisms Isolated from Various Sources", "Antibiotics Annual", Medical Encyclopedia Inc., New York: 329.

ROUNTREE, P. M., and THOMSON, E. F. (1949), "Incidence of Penicillin-Resistant and Streptomycin-Resistant Staphylococci in a Hospital", *Lancet*, 2: 501.

ROUNTREE, P. M. (1951), "Cross-Infection of Surgical Wounds", M. J. AUSTRALIA, 2: 766.

ROUNTREE, P. M., and BARBOUR, R. G. H. (1951), "Nasal Carrier Rates of Staphylococcus Pyogenes in Hospital Nurses", *J. Path. & Bact.*, 63: 313.

ROUNTREE, P. M. (1953), "Bacteriophage Typing of Strains of Staphylococci Isolated in Australia", *Lancet*, 1: 514.

SUMMERS, G. A. C. (1952), "Penicillin Resistant Staphylococci: Distribution among Out-patients", *Lancet*, 1: 135.

VOGELSANG, T. M. (1951), "The Incidence of Penicillin-Resistant Pathogenic Staphylococci Isolated from the Upper Respiratory Tracts of Young Healthy Persons", *Acta path. et microbiol.*, 29: 363.

WILLIAMS, R. E. O., RIPPON, J. E., and DOWSETT, L. M. (1953), "Bacteriophage Typing of Strains of Staphylococcus Aureus from Various Sources", *Lancet*, 1: 510.

AN ANALYSIS OF THE PHENOMENON KNOWN AS "CRITICAL CLOSING PRESSURE".

By A. J. CHRISTOPHERS,

Department of Pathology, University of Melbourne.

A PAPER by Burton (1951) entitled "On the Physical Equilibrium of Small Blood Vessels" deals with the theory of a paradoxical relation that exists between the distending pressure and the capacity of elastic tubes.

This relation is held to be the explanation of what he calls "the critical closing pressure" of small vessels. As his exposition of the theory is beyond the reach of those not equipped with the technique of higher mathematics, and as his exposition does not elucidate some of the fundamental principles involved, it is appropriate to attempt an exposition which is both simpler and more comprehensive.

According to the theory of elasticity, the length of an elastic thread is a continuous, positive, monotonic function of the tension of the thread. This means that, for any particular value of the tension, there is only one corresponding value of the length, and that an increase in tension always gives an increase in length.

These points are illustrated in the graphical representation of this functional relation by the curve always having a positive gradient.

Tensions Present in the Wall of a Distended Tube.

It can be shown from first principles (Grimsehl, 1932), for any cylindrical tube subject to a distending pressure, that the following relation holds between the distending pressure, the tension in the wall in the circumferential direction and the circumference of the tube, expressed algebraically:

$$p = \frac{2\pi t}{l} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where p, t, l are the measures of the distending pressure, the circumferential tension and the circumference respectively expressed in absolute units.

It can also be shown that the following relation holds between the distending pressure, the tension in the wall in

the longitudinal direction and the circumference of the tube, expressed algebraically:

$$p = \frac{4\pi T}{l} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

where T is the measure of the longitudinal tension.

It is apparent that the circumferential tension of the wall of a distended tube is twice the longitudinal tension:

$$t = 2T \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

The presence of this longitudinal tension is sometimes forgotten; but it will be remembered that, as the pressure distending a vessel increases, the vessel not only dilates but elongates also.

However, for the purpose of simplicity, we will ignore this elongation and suppose that we are dealing with tubes whose walls are elastic in the circumferential direction, but are rigid in the longitudinal direction; that is to say, with variation in distending pressure they will alter in calibre but not in length.

Derivation of Elastic Properties of a Tube from Knowledge of Elastic Properties of Its Walls.

Let us take a small section of a tube, of unit width such as would be left between two cross-sections unit distance apart. Cut this section in the longitudinal direction of the tube and then lay this strip out flat; this gives a flat strip of unit width and of length equal to the circumference of the tube.

We can now establish the elastic properties of this strip by varying the tension and measuring the lengths corresponding to the various tensions. By so doing we can determine the functional relation between the length and the tension, and we may represent this graphically by a curve. If we assume that the wall of the vessel is uniform, the elastic properties of all possible strips will be the same.

Let us now take a tube closed at both ends, in which the elastic properties of such circumferential strips are known, and we will follow the changes in the capacity of the tube as the distending pressure is changed.

The capacity of the tube is related to its cross-sectional area and its length according to the equation:

$$C = ad \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

where C, a and d are the measures of the capacity, cross-sectional area and length of the tube respectively.

Since the circumference of the tube corresponds to the length of the strips, we may calculate the cross-sectional area from the following equation:

$$a = \frac{l^2}{4\pi} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

By combining the last two equations, we may calculate the capacity from a knowledge of the circumference and the length of the tube according to the following equation:

$$C = \frac{l^2 d}{4\pi} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

Since the circumferential tension corresponds to the tension in the strips, the distending pressure may be calculated from a knowledge of the circumference and circumferential tension according to the equation:

$$p = \frac{2\pi t}{l} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

We have established by theoretical experiment the functional relation between the length of the circumferential strip (l) and the tension in this strip (t). Let this relation be given by the following equation:

$$t = f(l) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (7)$$

Substituting for t in equation (1) we get:

$$p = \frac{2\pi f(l)}{l} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8)$$

Now equation (4) expresses the capacity in terms of the circumference, and equation (8) expresses the distending pressure in terms of the circumference.

It is possible, therefore, through the medium of the circumference, to find the value of the distending pressure which corresponds to a particular value of the capacity. Thus the functional relation between the distending pressure and the capacity of the tube can be established theoretically.

Conditions Determining Whether Distending Pressure Will Increase or Decrease with Change in Circumference.

We have said that the distending pressure is proportional directly to the circumferential tension and inversely to the circumference according to the equation:

$$p = \frac{2\pi t}{l} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

Therefore, in order to assess the effect on the distending pressure of an increment in the circumference, one must sum (i) the direct effect of this increase in circumference, which will tend to diminish the distending pressure, and (ii) the effect of the concomitant increase in the tension, which will tend to increase the distending pressure.

If the increase in circumference is proportionately less than the increase in tension, the former effect will be outweighed by the latter, and a net increase in distending pressure will result. If the increase in circumference is proportionately greater than the increase in tension, a net decrease in distending pressure will occur. If the increase in circumference is proportionately equal to the increase in tension, there will be no change in the distending pressure.

Whether the increase in circumference is proportionately greater or less than the increase in tension may be demonstrated readily on the graph representing the elastic properties of a circumferential strip of the tube wall.

For theoretical simplicity we will consider first the case in which the elastic properties of such a strip are represented by a straight line as, for example, line PQ in Figure I.

Let us begin with the point plotting the tension against the length at point A on the line PQ, with the strip having a length of l units and a tension of t units. Suppose now that the length is increased by δl units and the tension increases thereby by δt units, and the plotting point moves from A to B.

The problem as to whether the increase in circumference is proportionately greater or less than the increase in tension may be solved in terms of the mathematical problem of whether $\frac{\delta l}{l}$ is greater or less than $\frac{\delta t}{t}$.

It is not difficult to show that, if the line PQ produced passes through the tension-axis, $\frac{\delta l}{l}$ will be greater than $\frac{\delta t}{t}$; whereas, if it passes through the length-axis, $\frac{\delta l}{l}$ will be less than $\frac{\delta t}{t}$.

Therefore for the case already shown in Figure I, where the line cuts the length-axis, an increase in circumference would be associated with a net increase in distending pressure. For the case shown in Figure II, where the line cuts the tension-axis, a net decrease in distending pressure would occur, and for the case shown in Figure III, where the line passes through the origin, there would be no change in distending pressure.

So far we have considered the cases in which the elastic properties of a circumferential strip are represented by a straight line. However, in practice, because materials obey

Hooke's law only within limited ranges, these properties would be represented not even in part by a straight line, but by a curve.

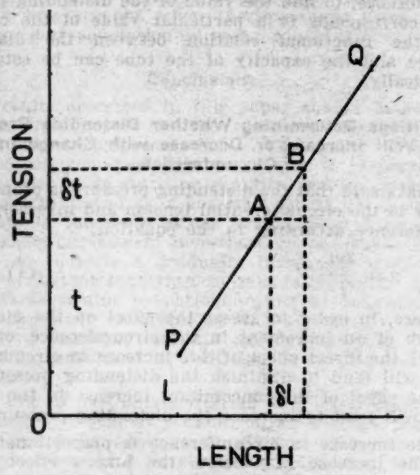

FIGURE I.

Graph showing one relation between tension and length of a strip of material having elastic properties. In these circumstances, with an increase of tension (δt) there is a smaller proportionate increase in length (δl). If we consider this length as the circumference of a tube, there is a disproportionate increase in tension; consequently the pressure within the cavity will be raised. Compare Figures II and III.

It is possible, however, using the infinitesimal calculus, to apply the same principles when the elastic properties of a strip are represented by a curve. It can be readily shown

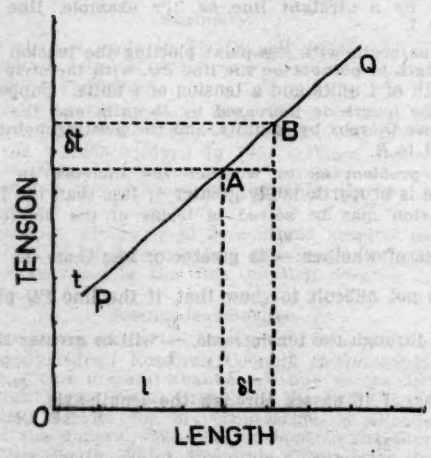

FIGURE II.

Graph showing another relation between tension and length of an elastic material. In this case, where the line *QP* will meet the ordinate a small increase in tension (δt) will cause a proportionately greater increase in length (δl). If we *transform this length to a circumference*, it will be seen that the increase in length is disproportionately greater than the increase in tension—that is, the pressure within the tube *will be diminished*. Compare Figures I and III.

that the effect of an increase in circumference upon the distending pressure varies according to whether the tangent to the curve passes through the tension-axis, the length axis or the origin.

For instance, if the elastic properties of a circumferential strip are represented by the curve in Figure IV, we can say that, at a length and tension represented by point

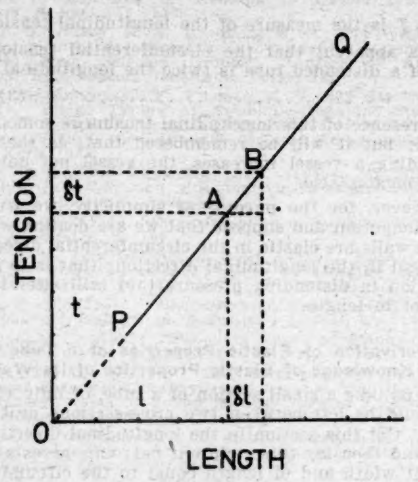

FIGURE III.

Graph showing a further relation between tension and length where the line *QP* passes through the origin. Here an increase in tension (δt) produces a proportionate increase in length (δl). When we transform this again to a tube it will be seen that there is no rise in pressure. Compare Figures I and II.

A on the curve, an increase in circumference will result in a net increase in distending pressure, for the tangent at *A* passes through the length-axis.

At a length and tension represented by point *C*, an increase in the circumference will give a net decrease in the distending pressure, as the tangent at *C* passes through

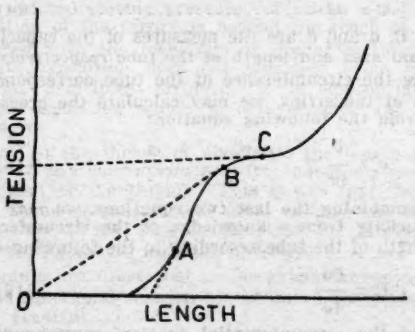

FIGURE IV.

Graph showing a line which is found by plotting the actual observation of tension against length in the case of elastic biological tissues. Here, Hooke's law is obeyed only with a limited radius, and a curve rather than a straight line is obtained. In *different parts of the curve it will correspond* respectively to the state of affairs shown in Figures I, II and III.

the tension-axis. At a length and tension represented by point B, an increase in the circumference does not alter the distending pressure, for the tangent at *B* passes through the origin.

The Paradoxical Situation.

A paradoxical situation arises when the tangent at a point passes through the tension-axis. Here a decrease in

circumference would give a net increase in distending pressure, and one would perhaps expect conversely that an increase in distending pressure would produce a decrease in circumference. We know that the last proposition is absurd.

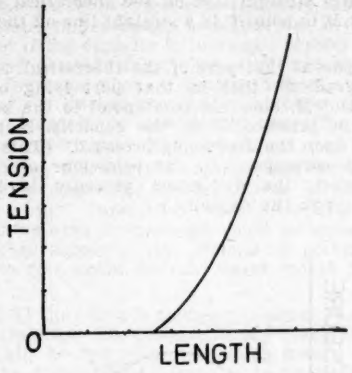

FIGURE V.

Graph showing the relation of tension to length. In all biological material, examined under conditions which correspond to ordinary ranges of physiological activity, this corresponds to the first part of the line shown in Figure IV. Compare Figure VI.

This paradox is difficult to solve theoretically; but it may be solved by studying the behaviour of such a tube in practice.

With perhaps one exception, the elastic properties of strips of biological material are represented by curves similar to the one shown in Figure V. These curves start from the length-axis and pass upwards with a convexity towards the length-axis, and the tangents from all parts of the curve all cut the length-axis.

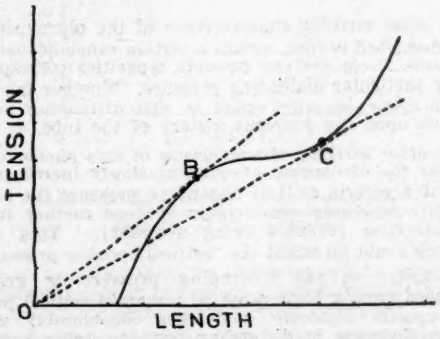

FIGURE VI.

Graph of a curve showing the elastic properties of muscle in the contracted state. Compare with Starling (1918a, Figure VIII).

The one notable exception to be considered is that of contractile tissue in its contracted state. For instance, the elastic properties of a contracted muscle are shown by a sigmoid curve similar to that in Figure VI. A somewhat similar curve for the elastic properties of contracted muscle is given by Starling (1918).

It can be seen that there is a portion of the curve from which the tangents cut the tension-axis, and this portion is bounded by the points *B* and *C* at which the tangents to the curve pass through the origin.

Elastic Properties of a Tube Formed by Contractile Tissue in Its Contracted State Theoretically Derived.

Suppose that we have a tube whose wall consists of contractile tissue in the contracted state, in which the elastic properties of a circumferential strip are represented by the curve in Figure VI.

If we plot on Figure VII the curve representing the theoretical functional relationship between the capacity of the tube and its distending pressure, we obtain a curve in which a portion lying between the points *L* and *M* has a negative gradient. This portion corresponds to that part of the curve in Figure VI lying between *B* and *C*.

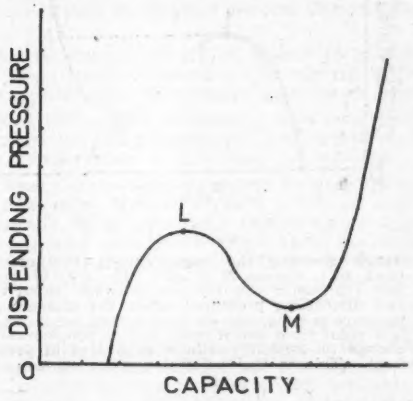

FIGURE VII.

Graph of a curve representing the elastic properties of a tube formed by contractile tissue in the contracted state, as derived theoretically.

How is this curve showing the theoretical relationship between the capacity and the distending pressure related to the curve showing this relationship as established by direct experiment?

Elastic Properties of a Tube Formed by Contractile Tissue in Its Contracted State Determined Experimentally.

Experimentally, we may make the distending pressure functionally dependent upon the capacity. This may be achieved by having control in the first place of the capacity, varying this progressively and noting the distending pressures developed at the various capacities.

If this is done, a curve is obtained that is identical to the one established theoretically, and it is found that for any one particular value of the capacity there is one and only one corresponding value of the distending pressure.

Alternatively, in the experiment we may make the capacity functionally dependent upon the distending pressure. This may be achieved by having control in the first place of the distending pressure, increasing (or decreasing) this progressively, and noting the capacities corresponding to the various distending pressures.

In Figure VIII the curve representing the functional relation between the capacity and the distending pressure established theoretically is shown by the continuous line with the portion between the points *L* and *M* having a negative gradient. The broken line traces the movement of the point plotting the capacity against the distending pressure as the distending pressure is progressively increased from zero.

As the distending pressure is progressively increased from zero, the point plotting the capacity against the distending pressure follows the curve established theoretically until it reaches point *L*. If the distending pressure is increased beyond the pressure corresponding to point *L* on the curve, the plotting point leaves the curve and moves

from *L* in a direction parallel with the capacity axis until it meets the curve again at point *N*, and thereafter it continues upwards along the curve.

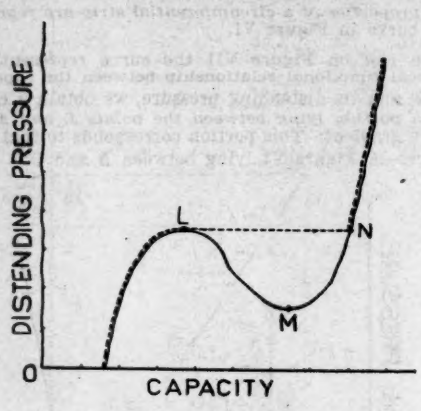

FIGURE VIII.

Graph showing the same curve (continuous line) as that seen in Figure VII. The broken line represents the relation between capacity and distending pressure; when the distending pressure is progressively raised from zero, there is a point from which there will be considerable change in capacity without alteration in pressure. This is the "critical opening pressure".

In Figure IX the curve representing the functional relation established theoretically is shown by the continuous line, whilst the broken line traces the movement of the point plotting the capacity against the distending pressure as the distending pressure is progressively lowered.

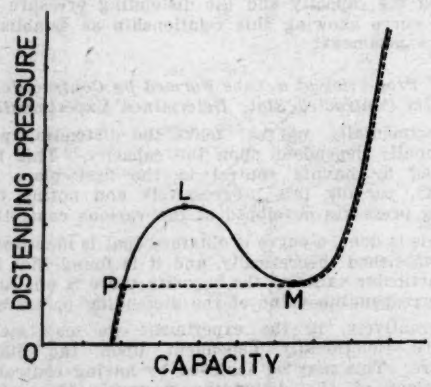

FIGURE IX.

Graph showing curve (continuous line) as that seen in Figure VII. The broken line represents a relation between the capacity and distending pressure; when the distending pressure is progressively lowered from a high value, there is a point at which there is a considerable change in capacity without alteration of pressure. This corresponds to the "critical closing pressure".

It will be seen that the plotting point follows the curve downwards again until it reaches point *M*. If the distending pressure is lowered beyond the pressure corresponding to point *M*, the plotting point leaves the curve and moves from *M* in a direction parallel with the capacity-axis until it meets the curve again at point *P*, and thereafter it proceeds along the curve again until it reaches the capacity-axis.

The possible movements of the point plotting the capacity against the distending pressure may be summed up as follows: (i) backwards and forwards along the theoretical curve from the origin of the curve to point *L*; (ii) backwards and forwards along the theoretical curve between point *M* and the end of the curve; (iii) from point *L* to point *M* in a straight line off the theoretical curve; (iv) from point *M* to point *P* in a straight line off the theoretical curve.

It is apparent that part of the theoretical curve with a negative gradient, that is, that part lying between the points *L* and *M*, does not correspond to the behaviour of the tube in practice when the capacity is functionally dependent upon the distending pressure. (This part of the curve does correspond to the behaviour of the tube in practice when the distending pressure is functionally dependent upon the capacity.)

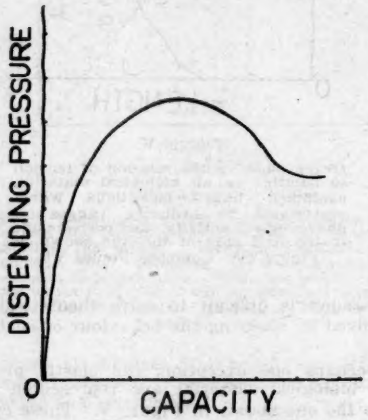

FIGURE X.

Graph of a curve representing the elastic properties of a contracted ventricle. See Starling (1918*b*, Figure VII).

The most striking characteristic of the phenomenon we have described is that, within a certain range of distending pressures, there are two possible capacities corresponding to any particular distending pressure. Whether the higher or the lower capacity exists at this distending pressure depends upon the previous history of the tube.

The other striking characteristic of this phenomenon is that, as the distending pressure is slowly increased from zero, at a certain critical distending pressure the capacity suddenly increases considerably without further increase in distending pressure being necessary. This critical pressure could be called the "critical opening pressure".

Similarly, as the distending pressure is gradually decreased from a high value, at a certain critical pressure the capacity suddenly diminishes considerably without further decrease in distending pressure being necessary, and this critical pressure could be called the "critical closing pressure". The critical opening pressure is always higher than the critical closing pressure.

These two pressures serve to mark the range of distending pressures over which the capacity is a two-valued function of the distending pressure.

Practical Applications of the Paradoxical Phenomenon.

This paradoxical phenomenon has arisen in physiology in two widely different situations. Lewis (1927) has shown that, after the small vessels of the human skin are subjected to the action of adrenaline, they may at certain high distending pressures be constricted or dilated according to whether this distending pressure was achieved by a progressive increase from a low value or a progressive

decrease from a much higher value of the distending pressure. The other occasion is when ventricular muscle is in the contracted state.

It is well known that the curve representing the relationship between the capacity and the distending pressure of a ventricle in its contracted state is of the form of that shown by the curve in Figure X (Starling, 1918). The maximum distending pressure is realized at a fairly high capacity, and if the capacity is increased beyond this point the distending pressure falls; that is, if the capacity of a ventricle is increased above a certain limit, the distending pressure realized during contraction becomes diminished. This limiting capacity is usually well above the capacities to which the ventricle is subjected.

If the relation between the capacity and the distending pressure for a contracted ventricle was investigated at exceedingly high capacities, the similarity to the phenomenon we have investigated would be more apparent. At still higher capacities the distending pressure would commence to rise again and the curve would be frankly sigmoid.

In Figure XI the curve is extended to show what happens at higher capacities. Such capacities are much higher than would normally be met with. In dealing with a contracted ventricle, the distending pressure is to be regarded as a function of the capacity, and the functional relationship between distending pressure and capacity established experimentally is identical to that relationship established theoretically. The phenomena of critical opening and critical closing pressures do not, therefore, arise.

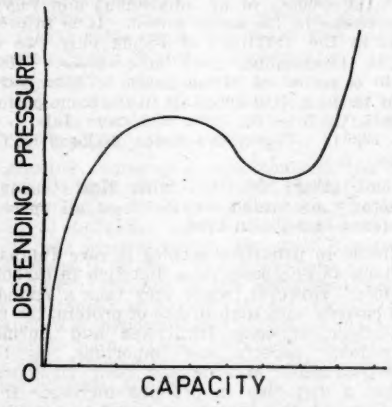

FIGURE XI.

Graph showing the curve as seen in Figure X, extended to show what occurs at higher capacities of the ventricle.

It is to be noted that the two occasions in which this phenomenon arises in physiology concern contractile tissue in the contracted state. This is very significant.

We have shown that the phenomenon arises only when the functional relationship between the circumference and the circumferential tension is represented by a sigmoid curve, in which there may be drawn two tangents to the curve from the origin.

The present state of knowledge in physiology shows that this type of curve is peculiar to the contracted state of contractile tissue and is shown by no other tissue.

It is also indicated strongly that only the first part of a curve, that part in which the slope of the curve is greater than the slope of a line joining a point of the curve to the origin, is significant. The remainder of the curve corresponds to distending pressures and capacities that are well outside those met with in practice.

This phenomenon will be shown by vessels whose walls consist of contractile tissue only when this tissue is in its contracted state and only at distending pressures that are well above those normally met with.

Summary.

It has been shown that the relation between the capacity and the distending pressure of a tube with elastic walls may be derived from a knowledge of the relation between the length and tension of elastic strips of which the tube may be considered to be composed.

It has been shown further that a paradoxical situation may arise in which an increase in capacity of the tube is associated with a decrease in distending pressure; this occurs when the relative increase in circumference of the tube is greater than the relative increase in circumferential tension.

It is a well known poperty of contracted muscle that, over a certain range of tensions, the relative increase in length is greater than the relative increase in tension.

Therefore, with a tube composed of such muscle arranged circumferentially, this paradoxical situation will occur over a range corresponding to this range of tensions.

It has been shown that the relation between the capacity and the distending pressure of such a tube as determined experimentally by progressively increasing or decreasing the capacity and noting the effect upon the distending pressure is exactly the same as the relation derived theoretically from a knowledge of the elastic properties of the walls.

However, the same relation, as determined experimentally by progressively increasing or decreasing the distending pressure and noting the effect upon the capacity, departs from the relation as derived theoretically, and this departure is responsible for the phenomena of "critical opening pressure" and "critical closing pressure".

As these phenomena are shown only by tubes whose walls are composed of tissue which will, over a range, show a greater relative increase in length than in tension, and as the only known tissues which have this property are contractile tissues in their contracted state, it follows that these phenomena will be shown only by tubes whose walls are composed of such tissues in such a state.

References.

BURTON, A. C. (1951), "On the Physical Equilibrium of Small Blood Vessels", *Am. J. Physiol.*, 164 : 319.

GRIMSEHL, E. (1932), "A Textbook of Physics, Volume 1—Mechanics", Blackie, London, 302.

LEWIS, T. (1927), "The Blood Vessels of the Human Skin and Their Responses", Shaw, London, 34.

STARLING, E. (1918*a*), "The Law of the Heart", Longmans, Green, London, 21, Figure VIII.

STARLING, E. (1918*b*), "The Law of the Heart", Longmans, Green, London, 20, Figure VII.

APPENDICITIS IN THE TROPICS AND ITS PITFALLS: A CLINICAL INVESTIGATION WITH REPORT OF TWO CASES.

By JAN J. SAAVE, M.D.,

Rabaul, Territory of Papua and New Guinea.

IT is known that the incidence, clinical characteristics and pathology of many cosmopolitan diseases in the tropics are greatly modified under local conditions (Manson-Bahr, 1945). This applies also to one of the commonest diseases elsewhere—appendicitis. This complaint appears to be rare among primitive peoples, or at least it is rarely recognized and treated.

The present communication gives an account of two known cases of appendicitis in New Guinea natives treated by me, and the discussion of a further 102 cases in which appendicitis was considered in the differential diagnosis.

Reports of Cases.

CASE I.—A male New Guinea native of Rabaul sub-district, aged approximately twenty-three years, was admitted to hospital on January 22, 1951, with severe abdominal pain in the right iliac fossa. He had felt a sharp, sudden pain in the "stomach" three days prior to his admission to hospital, and had passed frequent watery motions. On further questioning the patient admitted to having had an attack of generalized abdominal tenderness with nausea and rigor about a year earlier. However, it had subsided in approximately two weeks' time and he had been well since then. The patient admitted to taking partly European and partly native food.

On examination of the patient, his temperature was 99° F. The pulse rate was 110 per minute and the pulse was of fair volume, regular and equal; respirations were shallow and numbered 32 per minute. The blood pressure was 110 millimetres of mercury, systolic, and 75 millimetres, diastolic. The tongue was furred. The right pupil reacted more sluggishly to light than the left. Both pupils reacted equally to accommodation, but the right pupil was obviously larger when the eyes were at rest. There were rigidity and tenderness in Sherren's triangle and centralized pain five centimetres (two inches) below the umbilicus. Hyperæsthesia of the abdominal wall was greatly increased. The right upper and lower abdominal reflexes could not be elicited. Rovsing's sign and the obturator muscle sign were present. On auscultation peristaltic sounds appeared to be absent. Tympanites were heard on percussion. Rectal examination revealed acute, deep tenderness to touch, but there was no palpable mass in the pelvis. A blood examination gave the following information: the hæmoglobin value was 84%; the leucocytes numbered 6000 per cubic millimetre, 44% being neutrophile cells, 26% eosinophile cells, 4% monocytes, and 26% lymphocytes. A diagnosis of an acute abdominal emergency (possibly acute appendicitis) was made, and the patient was operated upon under general anæsthesia on the same day.

At operation, Battle's incision revealed a peculiarly shaped appendix lying over the brim of the pelvis. There was considerable enlargement of the lymph nodes at its base. The appendix was removed in the usual manner, the stump being covered with serosa (Lembert's) sutures. The customary purse-string suture was not applied in view of the lymphoid hyperplasia at the base and the possibility of secondary intussusception. The length of the organ was 92 millimetres (three and three-quarter inches); the width in its middle and lower third was 17 millimetres (approximately three-quarters of an inch) and nine millimetres (approximately three-eighths of an inch) in its upper third. The appendix was of peculiar shape, its distal portion being distended and club-shaped. Section disclosed an obvious narrowing of the lumen by a circular fibrotic scar. The entire distal part of the appendix resembled a hæmorrhagic infarct, being blue-red in colour and extensively swollen. The congested mucosa presented a few circumscribed ulcerated patches. However, the serous coat was found intact. The proximal part of the organ was œdematous, but otherwise not changed. Post-operative recovery was uneventful, and the patient was discharged from hospital, cured, on February 12. The post-operative diagnosis was obstructive appendicitis of intramural type.

The patient reported for subsequent examinations in December, 1951, and January, 1953; he was in good health.

CASE II.—A male New Guinea native of Rabaul sub-district, aged approximately seventeen years, was admitted to hospital on February 19, 1951, with acute generalized abdominal pain. Twenty-four hours prior to his admission to hospital he felt sudden and severe pain in the umbilical area. He was restless and constipated. He had not vomited. The patient admitted to having had easy access to European food.

On examination the patient was complaining of nausea. His temperature was 101° F. His pulse rate was 100 per minute, the pulse being of fair volume and irregular, but equal. Rigidity of the abdominal wall was present, but there was no definite guarding. The abdominal reflexes were absent. Pronounced tenderness to percussion was present over the right iliac fossa, and deep localized pain at McBurney's point on palpation. Rovsing's sign, the psoas sign and Sattler's sign were present. Rectal examination revealed slight tenderness. The patient was admitted to hospital for further observation with a diagnosis of an acute abdominal condition (possibly acute appendicitis). On the advice of a consultant he was given streptomycin, one gramme twice daily, and no food or fluid by mouth. On the next day (February 20) his condition had not improved. A blood count gave the following information: the hæmoglobin value was 90% and the erythrocytes numbered 4,720,000 per cubic millimetre; the leucocytes numbered 12,700 per cubic millimetre, 66% being neutrophile cells, 2% eosinophile cells, 8% monocytes, and 24% lymphocytes.

The patient was operated upon under local anæsthesia on the same day. At operation a gridiron incision was made in the right iliac fossa. A moderately inflamed retrocaecal appendix was easily removed. The usual purse-string suture was employed, and primary closure of the abdominal wall was carried out. The organ was congested and a few dilated subperitoneal blood vessels were present. The peritoneal sheen appeared to be normal. There were some fæcal concretions in the lumen. Post-operative recovery was uneventful. The patient reported for subsequent examinations in December, 1951, and December, 1952; he was enjoying good health.

There was some doubt whether the pathological lesions would justify the clinical findings. The specimen was therefore sent for histopathological examination. The following report was received:

> Histological examination of the appendix showed cloudy swelling and some denudation of the mucosal epithelium. Lymph nodes were hyperplastic and quite numerous neutrophile polymorphonuclears and eosinophiles were observed in the mucosa and submucosa. Vascular congestion was a prominent feature. The muscle layers and subserosa were infiltrated by a moderate number of eosinophiles and lymphocytes. It is considered that the findings were consistent with an inflammatory process.

Discussion.

There were 23,061 in-patients admitted to the Native Hospital, Rabaul, in the three-year period from January 1, 1950, to December 31, 1952. The two cases of appendicitis reported make 0·008% of all admissions and 1·08% of all major operations in the same period. It is interesting to know that in the Territory of Papua only two cases of appendicitis (Beaumont, 1908, and Boag, 1918) were reported in a period of fifteen years. There were 30,102 admissions to the native hospitals in the same period (from July 1, 1906, to June 30, 1909, and from July 1, 1912, to June 30, 1926). These two cases make 0·006% of all admissions.

Keusenhoff (1948) reported from East Germany that appendicectomy accounted for 18·4% of all operations in 1936 and for only 1·5% in 1946.

Appendicitis in primitive peoples is rare (Manson-Bahr, 1945) as long as they keep on a diet rich in carbohydrates and cellulose. However, when they take a mixed diet of European pattern with high intake of protein, the incidence of appendicitis increases (Schenken and Burns, 1948). The nutritional aspects are important, as the food influences pathogenic bacteria and their virulence. It is known that a diet rich in proteins increases the pathogenic activity of the organisms found commonly in the intestinal tract and has a definite effect on peristalsis. On the other hand, foods rich in cellulose act as peristaltic stimuli and lower the pathogenic activity of the bacteria (Finger, 1949). Ghyoot (1946) found appendicitis to be fairly frequent in Africans in the larger centres of the Belgian Congo; in 30% of all cases of appendicitis an appendiceal abscess was present. Peritonitis was present in 10% of cases.

The following short summary presents some of the diseases prevalent in the tropics which may be confused with appendicitis.

1. Intestinal amœbiasis. This closely resembles acute appendicitis or appendiceal abscess (Dennison and Dick, 1944). In nearly 80% of all appendices removed surgically in the Santo Tomás Hospital, Panama, amœbic lesions were found (Faust, 1951). Peritonitis as a fatal complication of amœbiasis may be confused with perforation of the appendix (Manson-Bahr, 1945).

2. Genito-urinary bilharziasis. This may be accompanied by acute appendicitis due to an accumulation of *Bilharzia hæmatobia* eggs in the appendix. Some patients require urgent surgical attention (Lovett-Campbell, 1948).

3. Paragonimiasis (endemic hæmoptysis). This may produce a confusing clinical picture.

4. Leptospirosis (Weil's disease). This may simulate acute appendicitis with its sudden onset and abdominal pain.

5. Enteric fevers. These may be clinically mistaken for appendicitis.

6. Relapsing fevers. These may resemble appendicitis in the pyrexial periods.

7. Spider poisoning. This produces a confused clinical picture (Faust, 1951).

8. Primary bubonic plague when the accompanying inguinal bubo is absent. This may be easily mistaken for appendicitis and the patient subjected to operation (Macchiavello, 1932).

9. *Lymphogranuloma venereum* (Nicolas-Favre disease) in the form of terminal ileitis. This may affect the large intestine and be confused with appendicitis (Crohn *et alii*, 1932; Soto-Rozas, 1952).

10. Subtertian malaria of gastro-intestinal type. This at times resembles acute appendicitis.

11. Intestinal worms. (*a*) *Tænia saginata* infestation of the appendix can produce symptoms of acute appendicitis, and the patient may be subjected to an emergency operation (Alfonso, 1937). At times the individual proglottids may be deposited in the lumen of the appendix and initiate acute appendicitis (Deschiens and Bablet, 1948). (*b*) *Ascaris lumbricoides* is known to invade the appendix, producing a confusing clinical picture. (*c*) *Enterobius* (*Oxyuris*) *vermicularis* is found in approximately 4% of all appendices removed in Cuba. The worms penetrate the submucous layer, but apparently do not produce any noticeable damage (Gordon, 1933). However, the pathogenic organisms become more active in their presence. Ashburn (1941) came to the conclusion that the pinworms are not ætiologically related to appendicitis.

The diagnosis of appendicitis is in many cases comparatively easy. There are, however, a number of cases in which a complex differential diagnosis must be considered. This applies especially to the tropics.

The following summary of symptoms in 102 cases well illustrates such difficulties. All 102 patients were adults aged between eighteen and thirty-five years. There were 71 males and 31 females. Abdominal pain was present in 99·9%. It was generalized in 46% and localized in the right iliac fossa in 53·9%. The other signs and symptoms were as follows: rigidity of the abdominal wall, 56·8%; signs of peritoneal irritation, 31·4%; rectal tenderness, 13·7%; and skin hyperæsthesia, 11·8%; nausea following the abdominal pain, 71·6%; vomiting, 55·9%; diarrhœa, 60·8%; elevated temperature, 67·6%; increased pulse rate, 66·7%; leucocytosis, 27·5%.

Summary.

Two cases of appendicitis in New Guinea natives with post-operative and histological findings are reported. The clinical data from 102 cases in which the symptoms resembled those of appendicitis are discussed.

Acknowledgements.

I am indebted to Dr. J. T. Gunther, Director of the Public Health Department, Territory of Papua and New Guinea, for his permission to publish this paper, and to Dr. B. R. V. Forbes, School of Public Health and Tropical Medicine, Sydney, for his histological report. I should like to thank Dr. C. Salemann for his help as a consultant.

References.

ALFONSO, J. R. (1957), *Rev. de med. trop. y parasitol. bacteriol. clin. y lab.*, 3: 225; quoted by Kouri, P., in "Clinical Tropical Medicine", by Gradwohl, R. B., *et alii*, *loco citato*.

ANDERSON, W. A. D. (1948), "Pathology", First Edition, Mosby, St. Louis: 842.

"ANNUAL REPORTS OF PAPUA", Reports on Medical Departments, Commonwealth of Australia, 1907-1909 and 1912-1926, Kemp, Victoria.

ASHBURN, L. L. (1941), "Appendiceal Oxyuriasis. Its Incidence and Relationship to Appendicitis", *Am. J. Path.*, 17: 841.

BEAUMONT, N. C. (1908), "Report on Medical Department", "Annual Reports of Papua": 88.

BOAG, F. L. (1918), "Report on Medical Department", "Annual Reports of Papua": 89.

CRAIG, C., and FAUST, E. C. (1951), "Clinical Parasitology", Lea & Febiger, Philadelphia, Fifth Edition.

CROHN, B. D., GINZBURG, L., and OPPENHEIMER, G. (1932), "Regional Ileitis. A Pathological and Clinical Entity", *J.A.M.A.*, 98: 1323.

DENNISON, W. M., and DICK, A. L. (1944), "Surgery in West Africa. Experiences in a Military Hospital", *J. Roy. Army M. Corps*, 82: 112.

DESCHIENS, R., and BABLET, J. (1948), "*Sur deux cas d'enclavement appendiculaire d'anneux de cestodes*", *Acta trop.*, 5: 219.

FAUST, E. C. (1951), unpublished data, quoted by Craig, C., and Faust, E.C., *loco citato*.

FINGER, J. (1949), "*Beitrag zur Appendicitis*", *Med. Klin.*, 32: 1017.

GHYOOT, E. (1946), "*L'appendicite chez les noires*", *Rec. trav. sc. méd. Congo Belge*, 5: 274.

GORDON, H. (1933), "Appendical Oxyuriasis and Appendicitis Based on a Study of 26,051 Appendixes", *Arch. Path.*, 16: 177.

GRADWOHL, R. B. H., BENITER SOTO, L., and FELSENFELD, O. (1952), "Clinical Tropical Medicine", Mosby, St. Louis, First Edition.

KEUSENHOFF, W. (1948), "*Die auffallende Abnahme der Erkrankungen an Appendicitis in den Kriegs- und Nachkriegsjahren*", *Deutsche GesundhWes.*, 3: 2.

LOVETT-CAMPBELL, A. C. (1948), "A Note on Bilharziasis in West African Troops", *Tr. Roy. Soc. Trop. Med. & Hyg.*, 41: 821.

MANSON-BAHR, P. H. (1945), "Manson's Tropical Diseases", Cassell, London, Twelfth Edition.

SCHENKEN, J. R., and BURNS, E. L. (1948), "The Gastro-intestinal Tract", in "Pathology", by Anderson, W. A. D., *loco citato*.

SOTO ROZAS, J. L. (1952), "Lymphogranuloma Venereum", in "Clinical Tropical Medicine", by Gradwohl, R. B. H., *et alii*, *loco citato*.

CARCINOMA OF THE PANCREAS.

By C. A. C. LEGGETT, M.S., F.R.A.C.S., F.A.C.S.,
Brisbane.

THERE is now the possibility of considerable surgical relief being available for patients with early carcinoma of the region of the head of the pancreas. Every effort should be made to make a reasonably early diagnosis. It is with these objects in view that the following observations are set out.

Pathology.

The various types of carcinoma occurring in the lower end of the biliary tract or in the head of the pancreas constitute one clinical group of cases, both as regards their clinical manifestation and as regards their surgical treatment. Except from the purely pathological point of view I can see no reason why attempts should be made to determine the exact site of origin of the carcinoma. Usually by the time that clinical symptoms are apparent, the exact site or origin of the carcinoma is not obvious. Patients with these lesions form one clinical group. There are four macroscopic manifestations of malignant disease of this area. The first is an ulcerative lesion of the duodenum in the region of the ampulla. The second is a papillary type of growth in this area. Thirdly there is a proliferative type of growth in the lower end of the common bile duct. Finally there is the hard scirrhous type of carcinoma of the head of the pancreas.

It is rare for a tumour in this area to give rise to a palpable tumour, although on one occasion I felt a mobile tumour in a very old and thin woman which proved to be a carcinoma of the head of the pancreas. This is very exceptional.

A few words should be said concerning the method of spread of a tumour in this area. Local infiltration is a pronounced feature, and extension along the lumen of the common bile duct commonly occurs. Warren Cole has reported finding carcinoma cells lying free along the main

pancreatic ducts. Lymphatic spread is usually fairly rapid, especially along perineural lymphatics. When it is remembered that the regional lymph nodes of the area lie in very close and intimate association with the pancreas, it can be readily understood how lymph node invasion is relatively early.

In my experience hepatic secondary deposits are rare at the time of operation; but occasionally bizarre metastases are demonstrated later in the course of the disease, and enlargement of the supraclavicular nodes is commonly seen.

Peritoneal deposits are a common manifestation of secondary spread, and of course are accompanied by a malignant ascites. Obstruction to the common bile duct is often not due to complete obturation or obliteration by pressure of the malignant tissue, because it is a common observation that in many cases examination of an excised operation or autopsy specimen shows that a duct space still exists, even though the clinical appearance of the jaundice suggests a complete obstruction. In addition, in the earlier stages, it is my experience that the jaundice can be fluctuating. There is, of course, dilatation of all the bile passages constituting hydrohepatosis, and the liver becomes clinically enlarged. If the gall-bladder has been in a reasonably healthy state prior to the onset of back pressure, it becomes enlarged and is often easily palpable. I think enlargement of the liver and dilatation of the biliary duct system are a cause of the constant aching pains so frequetly experienced by these patients. Secondary ascending cholangitis does occur, but is much less common than when the common bile duct is partially obstructed by the presence of gall-stones.

It must not be forgotten that obstruction of the main pancreatic duct arises in the same way as dilatation of the bile ducts, and just as there is some fibrosis of the liver there is considerable fibrosis of the body and tail of the pancreas. This often gives rise to a diffuse enlargement and pronounced increase in the hardness of the gland, so much so that at times I have had great difficulty in estimating whether the body of the pancreas is involved in the neoplastic process or not. On one occasion I was so convinced that the body of the pancreas was involved that I performed a total pancreatectomy when the patient suffered from a lesion limited to the periampullary area.

The Clinical Features of the Disease.

Of course, the onset of jaundice is by far the commonest way in which these patients are finally made to realize that they are seriously ill. However, in close questioning of these patients it is found that practically in every case there have been symptoms of definite degree preceding the onset of jaundice by many weeks or even months. Anorexia is one of the earliest symptoms that the patient notices, and this anorexia may precede jaundice by a number of weeks. It is intensified, of course, when jaundice becomes pronounced. The anorexia is often followed by a feeling of lack of well-being. The patient often complains of undue lassitude and tiredness, and says that he does not know what is the matter with him, but he is not feeling well.

Loss of Weight.

Loss of weight is sometimes pronounced when the patient presents for definite surgical treatment, and in my experience some degree of weight loss is almost universal. This is accounted for by the patient's appetite reaction to the abdominal discomfort, by the disordered absorption of fat, and by the voluntary dietary experiments on the part of the patient, more than by any direct effects of the metabolism of tumour cells.

Pain.

It is rare, in my experience, for the patient to complain of pain as severe as the pain of typical biliary colic due to cholelithiasis; but nevertheless, the pain is sometimes severe and is more of an aching type felt in the epigastrium, but also in the lower thoracic region posteriorly. Even in lesions in the area under discussion, in which jaundice is usually of fairly early occurrence, a diagnosis of functional dyspepsia or other functional disease is sometimes made in the pre-icteric stage.

I can remember an active man, aged sixty years, who was involved in domestic difficulties, but who complained of epigastric discomfort and backache, and who was thought by a discerning and senior physician to have a functional alimentary disturbance and osteoarthritis of the vertebral column.

These pre-icteric symptoms are of the greatest importance in making an accurate and early differential diagnosis. An irregular epigastric pain, at times definitely aggravated by food, is very common in this condition. The pain may be interpreted as a colic.

Jaundice.

It is not long, as a rule, before jaundice makes itself apparent. Most of these patients complain of pruritus before they notice the icteric changes in the skin and the presence of bile pigment in the urine. I have had one patient recently who consulted her doctor complaining of pruritus in addition to vague dyspeptic symptoms, and the physician made a positive diagnosis of functional disorder. Jaundice is as a rule slowly progressive in intensity, but it must not be thought that this is invariable.

I have recently seen a patient who had jaundice for four weeks and then all clinical evidence of jaundice disappeared for a number of weeks. Actually at the time of exploration the serum bilirubin level was only very slightly increased; but this patient had an extensive carcinoma of the head of the pancreas and no evidence of cholelithiasis.

As has been mentioned previously, infective phenomena do not occur very commonly with malignant growths in this area, but they are met with at times. Jaundice caused by periampullary carcinoma is rarely painless.

Bowel Disturbance.

Just as in pyloric stenosis the patient may emphasize the obvious disturbance of bowel function, so in carcinoma of the head of the pancreas there is a bowel disturbance, mainly consisting of diarrhœa with the passage of bulky stools containing an excess of fat. Such a diarrhœa always suggests a pancreatic lesion, and more frequently a carcinoma of the head of the pancreas rather than a lesion of the ampulla.

Depression.

The psychological outlook of the patient at the consultation gives the impression of a depressive psychological state. This miserable outlook is aggravated when the patient becomes jaundiced.

Vomiting.

Nausea and vomiting at irregular intervals after food are very common, but the patients usually do not emphasize these symptoms. Usually in these patients examination of the abdomen reveals the liver to be enlarged and slightly tender, and the gall-bladder is often enlarged and palpable.

Duration of the Disease.

The downhill course of the untreated patient after the onset of jaundice is not always very rapid. Some of these patients become very deeply jaundiced, but manage to exist in a most miserable fashion with anorexia, depression, pruritus and diarrhœa for as long as six months. However, the course of the disease may be very rapid. I have resected a carcinoma of the head of the pancreas in the belief that there were no obvious secondary deposits. The patient then died ten weeks later with a liver the site of gross secondary deposits.

Consideration of the Diagnosis.

Usually the important clinical problem is to determine whether the jaundice is obstructive in nature. The very greatest importance, of course, as in all cases, is a clear analysis of the history given by the patient. The onset of jaundice due to a carcinoma of the region of the head of the pancreas is characterized by a rather longer period of vague but definite pre-icteric symptoms; but in infective

hepatitis there is frequently an onset which is more clear-cut and suggestive of a systemic toxic disturbance for a much shorter period immediately prior to the onset of jaundice.

I usually rely upon the following tests as an aid in making my decision concerning exploration or not. I always carry out a serum bilirubin estimation to give a more accurate indication of the degree of jaundice. Then I ask for a serum alkaline phosphatase test, the result of which is usually greater than 30 units in obstructive jaundice, and another liver function test. One must emphasize, of course, that the earlier in the established case of jaundice these investigations are made, the more likely they are to give a clear help in their findings. One of the most valuable pre-operative estimations, of course, is the prothrombin level, and the response to the administration of vitamin *K* gives a very good idea of liver function.

The stools should be examined for the presence of occult blood (as well as for steatorrhœa), because occult blood is present as a rule when there is an ulcerative lesion of the ampullary region.

There was one very outstanding case of a man who was actually in hospital awaiting exploration for what was thought to be a carcinoma of the head of the pancreas when he had a fairly severe melæna. To me that was additional evidence of an ulcerative lesion of the duodenum, and that proved to be the case at operation.

I think that a radiological examination of these jaundiced patients is worth while. It is surprising how often one can see evidence of duodenal distortion in these cases. It is not often that the duodenum will be seen to be slanted as it is in the presence of a large retroperitoneal glandular mass, but there is often irregularity of the second part of the duodenum. Of course, if a barium meal X-ray examination is performed on a jaundiced patient, the radiologist should set out to get good exposures of the duodenum and especially the second part. If an investigation is being made in the pre-icteric stage, a full alimentary survey will be made in any case. Duodenal intubation may give further evidence by revealing pancreatic deficiency. This is a very useful and instructive survey when it is undertaken in special clinical units, but is not such a useful procedure in general practice.

Abdominal Exploration.

The patient should be prepared for operation in the usual way, it being remembered that protein and vitamin deficiencies are likely to be present. Of course, vitamin *K* should be given, and prothrombin times should be estimated before and during the administration of the vitamin *K*. This procedure gives a practical estimate of the liver function. Usually chemotherapy or antibiotic therapy is not necessary prior to operation. The blood transfusion service will require to have adequate blood supplies available in case an extensive procedure is feasible.

I think that operation should be advised in every case in which it is reasonably certain that the patient is suffering from obstructive jaundice. There may be some discussion and difference of opinion as to whether radical surgery or palliative surgery should be performed after exploration reveals the presence of a malignant lesion in this region; but I think there is no question that surgery should be advised when hepato-cellular disease cannot be diagnosed certainly. Especially is this so when it is remembered that obstruction of the lower end of the common bile duct can be due to a so-called silent gall-stone, and even at exploration it may not be clear whether the tumour felt at the lower end of the common bile duct is an impacted calculus or a neoplasm.

I would like now to speak of the exploration of the abdomen and the course that should be followed during that procedure. I favour a transverse invision; but I have performed pancreatic resections through adequate vertical incisions. When the abdomen is opened, if there are no ascites and no peritoneal deposits, the gall-bladder is inspected immediately. Usually the gall-bladder is found to be grossly dilated by thick dark bile, and when the enlarged liver is displaced upwards the common bile duct is inspected. It is usually greatly dilated except when it is filled by a proliferating carcinoma or when there is a carcinoma of the more proximal ducts. The common bile duct is palpated and may contain calculi even if a growth is present as well. Attention is given next to the alimentary tract. The stomach is examined, and if it is found normal, attention is directed to the duodenum. It is palpated and if necessary mobilized from the lateral aspect so that two fingers can be placed behind the duodenum. This allows a more adequate palpation to be carried out.

The pancreas or duodenum may be obviously the site of tumour formation. Even so, the lesser sac is opened next by incision of the gastro-colic omentum, and the body of the pancreas is palpated and inspected. Finally a general lower abdominal exploration is carried out. At the conclusion of this step attention is directed to investigation of the abnormality detected on palpation in the region of the head of the pancreas. I think that the common bile duct should be opened at this stage. It takes some time to aspirate the retained and partly inspissated biliary content until the common bile duct and gall-bladder are empty. It is wise to bear in mind when opening the common bile duct that it may be necessary to use it for the anastomosis. Some discretion is therefore necessary when choosing the position at which to incise the duct. I prefer the incision to be made as low as possible and as close as possible to the upper border of the duodenum. The lower end of the common bile duct is explored by probe, and if possible—and it often is possible—with the finger as well. At times a stone is discovered, and on other occasions an obvious growth in the lumen of the common duct. It may be that the probe will not pass to or through the papilla of Vater, and the next step is to open the duodenum.

The anterior wall of the second part of the duodenum is incised longitudinally. This incision should be adequate to give exposure of the papillary region. In my experience the duodenum is usually opened at a point rather proximal to the papilla. Small retractions are superior to the use of Allis forceps in giving adequate exposure. The area is inspected and palpated, and this step is aided by the manipulation of the probe in the common bile duct.

The diagnosis may be established at this stage. If it is not clearly apparent that the biliary obstruction is due to a malignant lesion, a difficult position arises: either the patient is submitted to a radical procedure carrying a high mortality for a lesion which may not be malignant, or an operable lesion is allowed to remain. I think a palliative operation is the procedure of choice if it is impossible to obtain further information. However, there are several methods of obtaining histological support for the next procedure.

Surface biopsy of the pancreas is a possible but very uncertain method. Needle biopsy of the pancreas is a method I have used and which I first saw used at the Mayo Clinic with success. Rodney Smith, of Saint George's Hospital, London, advises a transduodenal biopsy with an ophthalmic trephine. A combination of these biopsy methods will usually give the answer in the case which is suitable for resection. If an immediate histological report is available, one can proceed to a radical operation or a short-circuit of the biliary tract, whichever is indicated. If an immediate biopsy report is not available, it is wise to close the duodenum and perform either a cholecysto-enterostomy or a choledocho-enterostomy with an entero-anastomosis in a long loop. This will serve either as a suitable palliative operation or as a first-stage operation in a radical resection.

Finally, in the presence of a dilated common bile duct and no obvious evidence of tumour, it is obligatory to proceed as I have indicated previously, and perform a most thorough and systematic exploration.

Surgical Procedures.

I have deliberately not discussed the technical aspects of the surgical treatment of these lesions, because the difficult and differing problems which they set are of purely

surgical interest, and the aim and purpose of this article is a consideration of the clinical features of the disease.

Summary.

A short discourse is given on the pathology and clinical features of carcinoma of the pancreas. Stress is laid on certain features of the condition so that diagnosis may be facilitated. The frequency of the occurrence of pain is stressed. Details of the steps to be followed in the exploration of a patient with jaundice suspected of being due to a periampullary lesion are set out. A brief survey of the surgical procedures available for the relief of the condition is given.

References.

BRITNELL, E. S. (1952), "Technical Considerations in Resection of the Head of the Pancreas", *Surg., Gynec & Obst.*, 95 : 81.

CATTELL, R. B., and PYRTEK, L. J. (1949), "Appraisal of Pancreatoduodenal Resection: Follow-up Study of 61 Cases", *Ann Surg.*, 129 : 840.

CATTELL, R. B., and WARREN, K. W. (1953), "Surgery of the Pancreas".

DOUGLASS, B. E., BAGGENSTOSS, A. H., and HOLLINSHEAD, W. H. (1950), "The Anatomy of the Portal Vein and Its Tributaries", *Surg., Gynec. & Obst.*, 91 : 562.

MCDERMOTT, W. V. (1952), "A One Stage Pancreatoduodenectomy with Resection of the Portal Vein for Carcinoma of the Pancreas", *Ann. Surg.*, 136 : 1012.

MILLER, E. M., DOCKERTY, M. B., WOLLAEGER, E. E., and WAUGH, J. M. (1951), "Carcinoma in Region of Ampulla of Vater, Cases in which Resection was Performed", *Surg., Gynec. & Obst.*, 92 : 72.

SMITH, R. (1953), "The Surgery of Pancreatic Neoplasm".

RELAXANTS, WITH SPECIAL REFERENCE TO THE SUCCINYL-CHOLINES.[1]

By PHILIP WOLFERS, F.F.A.R.C.S., D.A.,
Melbourne.

"ANYONE who can put a needle into a vein can produce perfect relaxation nowadays." If that remark by a surgeon of repute was true in all its implications, there would be no society of professional anæsthetists to hear this address; and it is certainly true that profound paralysis is absurdly easy of achievement with the aid of relaxants. The fallacy, of course, lies in the safety or otherwise of the procedure.

I propose to mention three depressing accompaniments of this paralysis. They are: depression of respiration; depression of the oro-pharyngeal musculature; depression of sphincters. If the abdominal muscles are sufficiently relaxed to satisfy a surgeon operating in that region, then the respiration is sufficiently depressed to require assistance or control. While it is usually possible to maintain an adequate airway in a patient who has not received relaxants, the paralysis of the oro-pharyngeal muscles which accompanies their use frequently makes the problem an insoluble one until the trachea is intubated. The anæsthetist must therefore be competent and prepared to intubate the trachea. Depression of the cardiac and laryngeal sphincters makes possible regurgitation under anæsthesia; to combat this, tracheal intubation, suction and even bronchoscopy may be urgently needed at any time.

The Succinyl-cholines.

When *d*-tubocurarine, gallamine and decamethonium became available, the anæsthetist was able to satisfy the demands of the surgeon up to a point, but there was a gap in his armamentarium. A drug was required which would produce profound relaxation for very short periods. Such a drug would make possible the production of good relaxation for minor procedures performed in the out-patient department and allow the patient to return home quickly.

This gap was filled when Bovet and his colleagues found that very short-lived relaxation could be produced by the bis-choline esters of succinic acid. Like other relaxants, these compounds contain a quaternary ammonium group at each end. There are two groups in common use at present; in one, three methyl groups are linked to the ammonium radical at each end—this is the suxamethonium group; in the other, the suxethoniums, one methyl is replaced by an ethyl at each end.

The salts used as relaxants are the halides. The halide ion, being physiologically inert in such small concentrations, is responsible for very small differences in action, but does determine differences in molecular weight and therefore in dosage. Aqueous solutions of these compounds undergo slow hydrolysis and are best prepared just before use. Some of the salts are miscible with thiopentone and pethidine, but their activity rapidly falls off when they are mixed in this way.

Suxamethoniums.

The iodide was the first to be used. It was originally produced and investigated by Bovet in 1949 under the name of "370 IS", and was described by von Dardel and Thesleff at the 26th Congress of Anæsthetists. Patients are occasionally sensitive to the iodine ion; the drug is not miscible with thiopentone.

The bromide is prepared by May and Baker, Proprietary, Limited, under the name of "Brevidil 'M'". It is presented as a white powder which has to be dissolved just before use, as it is unstable in solution. It is freely soluble in water.

The chloride is prepared by Allen and Hanburys, Limited, as "Scoline" (succinylcholine chloride or diacetylcholine chloride). It is conveniently presented as a stable solution. It is miscible with thiopentone, but undergoes rapid hydrolysis when so mixed.

Suxethoniums.

The iodide was synthesized by Bovet under the name "362 IS" and is also known as tachycurine and celocurine. It was investigated by Ottolenghi, Manni and Mazzoni, who found that it has some effect on smooth muscle also. Like suxamethonium iodide, it is not readily soluble and not miscible with thiopentone.

The bromide is prepared by May and Baker, Proprietary, Limited, as "Brevidil 'E'".

Relative Action.

Comparative studies of these compounds have been carried out at Saint George's Hospital, London, and elsewhere. Except for their difference in potency, the "methonium" ion being 1·6 times as potent as the "ethonium", little difference in their activity or toxicity has been observed. However, Manni and Mazzoni state that the rise in blood pressure and fall of pulse rate which are sometimes seen with the suxamethonium compounds do not occur with suxethoniums. As the paralysing activity of the drugs depends on the active cation and not on the whole molecule, their potency should be compared by the relative content of cation.

Mode of Action.

The exact mode of action of these relaxants is still not quite clear, but it can be said that, like decamethonium iodide, the result of their action is depolarization at the myo-neural junction with consequent paralysis. This depolarization is the result either of the direct action of the drug on the motor end-plate or of inhibition of cholinesterase activity, with a consequent prolongation of the normal action of acetylcholine on the myo-neural junction owing to a rise in its concentration. In other words, it may be a competitive inhibitor of acetylcholine hydrolysis. In either case, it seems likely that the short duration of its effect is due to its rapid destruction by the plasma pseudocholinesterase.

[1] Based on a paper read at a meeting of the Victorian Branch of the Australian Society of Anæsthetists on March 27, 1954, at Ballarat.

Mode of Destruction.

The compounds are rapidly broken down in the body to succinic acid and choline. The exact method is uncertain. Bovet believed that the drugs were destroyed at the myo-neural junction by the cholinesterase there, but it has since been shown by Evans, Gray, Lehmann and Silk that the esterase in the blood cells plays no part. They claim that the plasma esterase is alone responsible. To support this view, many reports have appeared of a low plasma pseudocholinesterase level in patients showing prolonged apnœa after "Scoline".

Thus, as was pointed out by Hall, Lehmann and Silk, the action of these drugs can be visualized as a combination of them with two cholinesterases. True cholinesterase *plus* drug leads to depolarization and relaxation; pseudocholinesterase *plus* drug leads to inactivation of the drug and return of muscular power.

Suitability for Use in Anæsthesia.

Having been satisfied that these drugs do produce good relaxation, are rapidly destroyed and are relatively non-toxic, the anæsthetist may next be concerned with the question of their muscle-specificity: which muscles are most sensitive to the drugs? Do they spare respiration? When an ordinary dose of "Scoline" is given as a single injection, complete relaxation of all muscles occurs. But if the drug is given sufficiently slowly, its muscle-specificity can be shown to be the same as that of curare. This was demonstrated by the auto-experiments of Otto Mayrhofer, who used suxamethonium chloride.

In practice we have found that satisfactory abdominal relaxation can be obtained with "Scoline" while some diaphragmatic movement is retained. But the drug can make no claims to sparing respiration. However, I believe that this quality has been over-emphasized, as some assistance to respiration is always necessary when a relaxant has been given in sufficient dosage to relax the abdominal muscles.

Dosage.

No two anæsthetists will agree on the correct dose to give to a patient to produce a particular result, or even on the basis whereon the dose should be calculated. Weight, age and metabolic activity are the usual criteria on which drug dosage is based; but when the depolarizing group is used, it seems that little reliance can be placed on such factors. For this reason it may be wise to begin with small doses.

It is impossible to foretell the duration of apnœa; similarly, one cannot estimate with any accuracy the quantity of drug which will be required to produce one hour's relaxation by the drip method. The continuous administration of "Scoline" was used in a series of 250 patients, and the dosage has varied from two to 16 milligrammes per minute. The three factors which have seemed to influence dosage are the state of the liver, the general nutrition and the blood volume. It is well recognized that low pseudocholinesterase levels are found in hepatic disease and malnutrition; in the group of patients operated on for bowel obstructions, the average was 4·7 milligrammes per minute. The over-all average was 6·4 milligrammes per minute. Many of the patients with obstructions had carcinoma and were in a poor state of nutrition. The drugs should also be treated with respect after severe hæmorrhage.

Some alarm has been caused by the many reports of prolonged apnœa following "Scoline". In the majority of these the apnœa occurred in healthy patients, and in only a few was a low pseudocholinesterase level found. In two of these cases apnœa followed the administration of neostigmine, and there the cause seems clear; but the others have not been fully explained. There is one factor common to many of these reports—that is, the administration of large doses of relaxant and thiopentone. It is unlikely that 75 to 100 milligrammes of "Scoline" will produce apnœa for longer than five to ten minutes in the presence of a normal pseudocholinesterase level; but it is possible that with these doses the respiratory paralysis lasts long enough for the anæsthetist unwittingly to produce acapnia in the heavily premedicated patient. The administration of carbon dioxide instead of neostigmine, nikethamide or picrotoxin might have saved a great deal of anxiety. Other causes which have been suggested for the phenomenon include over-distension of the lungs leading to inhibition of the Hering-Breuer reflex, and partial hydrolysis of the drug to succinylmonocholine, a relaxant of considerably longer action. If large doses of thiopentone are given with the "Scoline", the dose should be reduced, as thiopentone without doubt prolongs its action. This is believed to be due to inhibition of cholinesterase activity by thiopentone.

Gray, Evans, Lehmann and Silk have reported the successful use of "cholase", a preparation of human pseudocholinesterase, for shortening apnœa following the short-acting relaxants. Although this drug would rarely have to be used, its availability would make the anæsthetist happier when he was using these drugs in "poor risk" patients. If "cholase" is unavailable, fresh blood transfusion is of value.

Side Effects.

When they are given in reasonable doses, these drugs appear to have no deleterious side effects. Volunteers who have had them administered while conscious report that, apart from the painful twitchings and the unpleasant experience, they noticed no impairment of mental processes or sensation, and no after-effects.

Stiffness and aching in muscles has been, in my experience, a fairly common complaint after recovery from these relaxants when they are given rapidly. Since a similar phenomenon is occasionally met in ambulant patients who have received gallamine, and since the incidence of symptoms seems to bear no relation to the severity of the fibrillation of the depolarization phase, it seems likely that some residual effect on the myo-neural junction is responsible, rather than trauma during depolarization.

Bovet was unable to demonstrate any blocking effect on the autonomic ganglia, although large doses in the dog and cat produced stimulation of the gut. The effect of these drugs on the blood pressure, especially when they are used as a continuous infusion, has raised some interest. Calvert and Morgan "consider that suxamethonium has no direct pressor action"; Bourne states that "Scoline" as a single dose with adequate ventilation produces no effect on the blood pressure; but if it is given as a continuous infusion, a proportion of patients show a "climbing" blood pressure which may reach 200 millimetres of mercury, systolic. We have not experienced this dramatic type of rise; but in about 25% of cases there is a rise of 10 to 20 millimetres of mercury. There are two possible causes for this rise, as follows: (i) Accumulation of carbon dioxide due to under-ventilation. We have taken care that this cannot be incriminated in my series of cases. (ii) Direct action of the drug on autonomic ganglia.

Bourne, Collier and Somers suggest that stimulation by a nicotine action is responsible, and this seems the most likely explanation. At any rate, any dramatic effect should be avoidable by attention to dosage, and I do not believe that it is necessary to add hexamethonium bromide to the solution, as has been advocated in one quarter.

The action on the heart seems to be minimal. In a series of 150 electrocardiographic recordings on patients receiving the drugs for electroconvulsive therapy, we could find no change attributable to them except for an occasional slowing of the pulse rate. The blood pressure rise occasionally seen was not accompanied by electrocardiographic changes.

The action of these drugs on the internal organs seems to be of little significance. When an infusion of "Scoline" is used, the human gut seems unaffected; the intestines remain small and active. Profuse salivation occurs often with the drugs and lachrymation seldom.

Practical Aspects.

There are three procedures which at first sight seem ideal for the use of these drugs. These are intubation of the trachea, orthopædic manipulations and electroconvulsive therapy.

Intubation.—Forty to 60 milligrammes of "Scoline" will produce temporarily ideal conditions—a quiet patient, a relaxed jaw and cords so inviting that even the most timid student could scarcely fail to pass a Magill tube. It is beyond this stage that the drugs may fail the unwary. No sooner is the anæsthetist congratulating himself on his skill than the relaxant wears off, and it becomes evident that the plane of anæsthesia is too light. The patient begins to "buck" and bronchial spasm occurs, so that no more inhalational anæsthetic can be introduced. The rest of the operation is spent trying to correct this result. Some anæsthetists have returned to gallamine for intubation because of this risk. If intubation is to be carried out under one of these drugs, the anæsthetist must repeat the dose after intubation, or the patient must be well anæsthetized before the relaxant is injected, or the cords must be well cocainized.

Orthopædic Manipulations.—For most orthopædic manipulations, a dose of three to four milligrammes per stone with 250 milligrammes of thiopentone is sufficient. The dangers to be avoided are dislocations and fractures. Provided the patients are accompanied, they may be allowed to leave the hospital an hour after recovering consciousness.

Electroconvulsive Therapy.—These drugs are undoubtedly the drugs of choice for electroconvulsive therapy. I have used both the suxamethonium and the suxethonium drugs and find little to choose between them. "Brevidil 'E'" gives a shorter period of apnœa and paralysis, but its effect is somewhat less reliable than that of "Scoline" or "Brevidil 'M'". The patients are premedicated with atropine. They are given about 250 milligrammes of thiopentone followed by 0·7 milligramme per kilogram of "Scoline" or 1·3 milligrammes per kilogram of "Brevidil 'E'" through the same needle. These doses are adjusted for subsequent treatments.

Endoscopic Examinations.—The drugs have also proved useful for endoscopic examinations, especially diagnostic bronchoscopy. The patient is premedicated with atropine and given an amethocaine or lignocaine lozenge to suck ten minutes before leaving the ward. Sleep is induced with thiopentone, and a large dose of "Scoline"—up to 100 milligrammes—is given. The trachea is sprayed with a regional analgesic and the patient's lungs are well inflated with oxygen. The examination is carried out with oxygen running down the side tube of the bronchoscope. In spite of apnœa, the patient's colour remains pink for a surprisingly long time; if hypoxia is feared, good oxygenation can be obtained by manual pressure on the thoracic cage or by intubation of the bronchoscope.

In an attempt to explain why oxygenation is maintained so long under "Scoline" apnœa, we have carried out some oxygen consumption experiments. In all of a series of six cases, a decrease of at least 20% in consumption was shown with the cessation of respiration in the already anæsthetized patient.

In Abdominal Surgery.—Three techniques have been used in abdominal surgery. (i) These drugs may be given at the end of the operation for closure, a longer acting relaxant having provided the main relaxation. (ii) Intermittent injections may be used. (iii) A continuous infusion may be given. The first procedure is not favoured, as it is not a good principle to mix medicines in this way, and occasionally good muscle tone has not returned by the end of the operation. One does not then know whether or not to use neostigmine. The second method is tedious and difficult for prolonged procedures. The third method has proved very satisfactory for abdominal surgery. Von Dardel and Thesleff first described the use of the drugs in this way. They used suxamethonium iodide in 0·1% solution and found that two to three milligrammes per minute produced satisfactory relaxation. We have found 0·1% or 0·2% "Scoline" satisfactory, as it gives adequate control without over-infusion. The solution should be freshly prepared, as its activity deteriorates rapidly, and may be made up in normal saline, dextrose with 0·18% saline or dextran, according to the patient's requirements. "Brevidil 'E'" has not been found very suitable for use in this way, as much stronger solution and higher dosage are required. Anæsthesia is induced with thiopentone, and intubation carried out after relaxation has been obtained with "Scoline" and the cords well cocainized. Anæsthesia is maintained with nitrous oxide and oxygen, alone or with additional analgesics. In the majority of cases, no additional analgesic is needed.

In a series of 250 upper abdominal operations on adults, the mean requirement of "Scoline" was 6·4 milligrammes per minute, or about 0·1 milligramme per kilogram per minute. However, the variation in dosage was considerable. Most other writers have found a smaller mean dosage of relaxant sufficient, but they have made more use of other drugs as supplement. A minimal effective dosage is soon established and persisted with. Occasionally a progressive lowering of the drip rate required for relaxation is observed, possibly attributable to the failure of pseudocholinesterase production to keep pace with its destruction.

It is, of course, necessary to assist respiration while relaxation is present. I feel that it is important to preserve some slight respiratory movement, as otherwise it is very easy to give an over-dose, and the possibility of the patient's awakening during the operation is reduced. When "Scoline" is used in this way, very satisfactory operating conditions are produced with a minimum of narcotic and analgesic agents. One can also control the degree of relaxation in a way which is impossible with any other technique. The relaxation can be very profound for peritoneal closure, and yet good muscle power may be obtained five minutes later.

The post-operative condition of the patients has been very encouraging. Recovery of consciousness in the operating theatre is the rule; this, together with the rapid return of normal muscle tone, enabling the patient to maintain his own airway, makes the journey back to the ward much less hazardous. The ward sisters are able to have the patient sitting up and cooperating early.

There are obvious disadvantages to a technique which necessitates the setting up of an intravenous infusion apparatus and the whole-time assistance of respiration, but the advantages in this case can be considerable. The rapid control of relaxation makes the procedure exacting and interesting, and the dramatic return of normal muscle tone can be a revelation.

Post-operative muscle pain does not occur after this technique, owing either to the absence of a fibrillatory phase or to the later ambulation of these patients.

Acknowledgements.

I wish cordially to acknowledge the large contribution to this work of my colleagues at Saint George's Hospital, in particular Dr. R. A. Green.

References.

BOURNE, J. G., COLLIER, H. O. J., and SOMERS, G. F. (1952), "Succinylcholine: Muscle Relaxant of Short Action", *Lancet*, 1: 1225.

BOVER, D., BOVET-NITTI, F., CUARINO, S., LONGO, U. G., and MAROTTA, I. V. (1949), *Rendic. Ist. super. san.*, 2: 106.

CALVERT, R. J., and MORGAN, D. K. (1954), "Effect of Suxamethonium on Blood Pressure", *Anæsthesia*, 9: 196.

COLLIER, H. O. J., and MACAULEY, B. M. (1953), "Succinylmonocholine", *Brit. M. J.*, 1: 1280.

DAY, B. L. (1952), "Prolonged Apnœa", *Brit. M. J.*, 2: 162.

EVANS, F. T., GRAY, P. W. S., LEHMANN, H., and SILK, E. (1952), "Sensitivity to Succinylcholine in Relation to Serum Cholinesterase", *Lancet*, 1: 1229.

EVANS, F. T., GRAY, P. W. S., LEHMANN, H., and SILK, E. (1953), "Effect of Pseudocholinesterase Level on Action of Succinylcholine in Man", *Brit. M. J.*, 1: 137.

GRANT, G. (1952), "Prolonged Apnœa", *Brit. M. J.*, 1: 1352.

GREEN, R. A. (1953), "Controlled Relaxation with Succinylcholine Chloride", *Anæsthesia*, 8: 52.

HALL, L. W., LEHMANN, H., and SILK, E. (1953), "Response in Dogs to Relaxants Derived from Succinic Acid and Choline", *Brit. M. J.*, 1: 134.

HARPER, J. K. (1952), "Prolonged Apnœa", *Brit. M. J.*, 1: 866.
HEWER, C. L. (1952), "Prolonged Apnœa", *Brit. M. J.*, 2: 971.
HURLEY, M. J., and MONRO, A. B. (1952), "Prolonged Apnœa", *Brit. M. J.*, 1: 1027.
MAYRHOFER, O. K. (1952), "Self Experiments with Succinylcholine Chloride", *Brit. M. J.*, 1: 1332.
OTTOLENGHI, R., MANNI, C., and MAZZONI, P. (1952), "New Short Acting Curarising Agent", *Anesth. & Analg.*, 31: 243.
VON DARDEL, O., and THESLEFF, S. (1952), "Clinical Results with Succinylcholine Iodide, a New Muscle Relaxant", *Anesth. & Analg.*, 31: 250.
WILLIAMS, J. E. (1952), "Observations on the Use of "Scoline" as a Muscle Relaxant", M. J. AUSTRALIA, 1: 818.
WOLFERS, P. (1952), "Prolonged Apnœa", *Brit. M. J.*, 2: 778.
WOLFERS, P. (1953), "Brevidil 'E' in ECT", *Anæsthesia*, 8: 49.

A NOTE ON THE INCIDENCE OF CHOLELITHIASIS.

By R. A. JOSKE, M.D.,[1] E. G. SAINT, M.D.,[1] F. J. BROMILOW, M.Sc., Ph.D., and E. S. R. HUGHES, M.D., M.S.

From the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Victoria

THE incidence of cholelithiasis reported from different centres at different times has varied greatly. The reasons for this are unknown, although both genetic and acquired factors have been invoked, and it is possible that comparative geopathological studies will throw light on the problem.

This paper reports the incidence of cholelithiasis in 3685 routine post-mortem examinations performed at the Royal Melbourne Hospital during the years 1945 to 1950 inclusive. Patients who had had cholecystectomy performed during life have not been included, as the indications for operation and the operative findings were unavailable in most instances. This means, however, that the incidence of cholelithiasis reported here must be regarded as minimal. Variations in the incidence of cholelithiasis at different ages and in the two sexes have also been analysed.

The figures show only the total incidence of cholelithiasis and give no indication whatsoever of the frequency of symptoms referable to biliary disease or of the relative incidence of different types of gall-stone.

Results.

The results obtained are shown in Table I. These figures show cholelithiasis to be common in this community, for it was present in 551 of the 3685 autopsies, an incidence of 14·9%.

Age Incidence.

The distribution varied greatly with the age of the patient. Cholelithiasis was rare in young persons, but the incidence increased rapidly with advancing years and was greatest in elderly patients. It was present in only 17 of 495 patients under the age of forty-five years (3·5%), but was found in 301 of 1565 (19·2%) of those aged sixty-five years or more.

This increase in the frequency of cholelithiasis with increasing years is a general finding in most reported series (Crump, 1931; Dessau, 1943), although not all (Ryerson, 1911). Many cases of cholelithiasis in children have been reported (Potter, 1928; Seidler and Brakeley, 1940; Ulin *et alii*, 1951), including one in a baby which died six hours after delivery (Spence, 1941); but clinical practice and published statistics agree that cholelithiasis is seen with much greater frequency in middle-aged and elderly patients (Gross, 1929; Bockus, 1946).

Sex Incidence.

There was also a much greater incidence in females than in males. Cholelithiasis was present in 302 of 1486 females (20·3%), but in only 249 of 2199 males (11·3%). This difference is significant, and in our material gall-stones were approximately twice as common in females as in males, a finding in accord with clinical experience. This preponderance in females was found in all age groups studied, and the proportion of females to males was similar in all. Although only two of 254 (0·8%) males aged under forty-five years had cholelithiasis, the condition was present in 15 of 241 (6·2%) females of comparable age. In elderly patients aged sixty-five years or more, 150 of 991 males (15·1%) and 151 of 574 females (26·3%) were found to have gall-stones.

TABLE I.

The Incidence of Cholelithiasis in 3685 Routine Post-mortem Examinations at the Royal Melbourne Hospital, 1945 to 1950, Classified According to Age and Sex.

Age Group. (Years.)	Males.		Females.		Both Sexes.	
	Total Subjects.	Number with Gall-stones.	Total Subjects.	Number with Gall-stones.	Total Subjects.	Number with Gall-stones.
0 to 24	61	0	65	2 (3·1%)	126	2 (1·6%)
25 to 34	60	1 (1·7%)	60	2 (3·3%)	120	3 (2·5%)
35 to 44	133	1 (0·8%)	116	11 (9·5%)	249	12 (4·8%)
45 to 54	345	24 (7·0%)	272	48 (17·7%)	617	72 (11·7%)
55 to 64	609	73 (12·0%)	399	88 (22·0%)	1008	161 (16·0%)
65 to 74	579	75 (13·0%)	347	84 (24·0%)	926	159 (17·2%)
75 and over	412	75 (18·2%)	227	67 (29·5%)	639	142 (22·2%)
Total	2199	249 (11·3%)	1486	302 (20·3%)	3685	551 (14·9%)

The greater frequency of cholelithiasis in women has been observed in other reported series (Gross, 1929; Hamilton, 1932; Ludlow, 1937; Bockus, 1946; Becker and Chatgidakis, 1952; Cooke *et alii*, 1953).

These results are important, for they support the contention, first put forward by Gross (1929), that there is little relation between parity and the occurrence of cholelithiasis. If such a relation existed, the preponderance of female over male patients with cholelithiasis should increase with increasing years. This increase, however, has not been observed in this or other series (Gross, 1929; Hamilton, 1932; Dessau, 1943).

Geographical Incidence.

Only two other reports of the incidence of cholelithiasis have appeared in this country, both from South Australia. Hamilton (1932) reported the findings in 1000 autopsies performed between the years 1925 and 1929. Cholelithiasis was present in 106 (10·6%), which is rather lower than the present figure of 14·9%. Hamilton also found a slight preponderance in females, although not so great as that observed in this series. He recorded the frequency in females as 11·6% and in males as 10·1%.

Cleland (1943) studied the results of 7000 post-mortem examinations performed during the years 1920 to 1948. The number of cases of cholelithiasis was 871 (12·4%);[1] women were affected approximately twice as often as men, and the age incidence was also similar to that of Hamilton (1932) and the present series.

It is of interest to compare these Australian figures with those reported from other countries. In the United Kingdom similar reports have been published by Gross (1929) from Leeds, and by Cooke *et alii* (1953) from

[1] Working with the aid of a grant from the National Health and Medical Research Council of Australia.

[1] This figure was incorrectly stated to be 8% in the original paper.

London. Gross studied 9531 autopsies performed during the years 1910 to 1926 inclusive. She found the incidence of cholelithiasis to be 8·4%, increasing steadily with age and about twice as great in women as in men. Cooke *et alii* studied the reports of 3113 autopsies performed at Hammersmith Hospital during the years 1941 to 1950 and found cholelithiasis in 231 (7·4%).

The differences between Australian and United Kingdom figures are significant, and suggest strongly that cholelithiasis is much more common in this country, although the age and sex ratios are similar in both.

Reports from Europe and America are numerous, and the recorded frequency of cholelithiasis varies greatly. In western Europe the reported figures range from 4·4% to 12% (Gross, 1929), while in the United States of America the reported frequency varies from 7·0% (Ludlow, 1937) to 20·9% (Dessau, 1943), although this last series included chiefly patients aged over forty years.

Discussion.

The reasons for these variations in the incidence of cholelithiasis are not known.

There is some evidence that racial factors may be important and that the white race is more liable to gallstones than are coloured races. In South Africa gallstones are six times more common in Europeans than in the Bantu (Becker and Chatgidakis, 1952), and in the United States of America Jaffé (1933) found cholelithiasis less common in coloured patients than in whites. A low incidence has also been reported in Koreans (Ludlow, 1930) and in Chinese and Japanese (see Becker and Chatgidakis, 1952). Though these results may be affected by dietetic factors and the age composition of the populations studied, they suggest that genetic factors are important in the ætiology of cholelithiasis. This is also seen in the relation between cholelithiasis and familial diseases such as familial hypercholesterolæmia and essential hyperlipæmia. However, the similar age and sex ratios found in Australia and the United Kingdom would indicate that, even in genetically similar populations, acquired factors may alter the incidence of cholelithiasis, so that the final frequency depends upon both genetic and external influences.

Of the possible acquired causes of cholelithiasis, most attention has been paid to the possible metabolic effects of pregnancy and diet. There is now considerable evidence that pregnancy is not a causal factor in cholelithiasis, a point already mentioned. The low incidence of cholelithiasis in coloured races with a higher birth rate than whites further supports this contention.

It is not possible to assess the role of dietetic factors. There is insufficient published information and further work on this problem is needed. Some authors report a higher incidence in well-fed people (English, 1927), others in those with poor diets (Mosher, 1901).

There is some evidence that the frequency of cholelithiasis is increasing. Comparative figures from the same area at different times are sparse, but in Adelaide Cleland (1953) found the incidence greater in the later than in the earlier part of his series, and Dessau (1943) made similar findings in Boston. The increase affects all ages and both sexes, but is more pronounced in males, so that the sex difference may be gradually diminishing. This is borne out by the figures from the United Kingdom (Hurst, 1923; Gross, 1929) and from the United States of America (Mitchell, 1918; Jaffé, 1933; Dessau, 1943).

Summary.

1. The incidence of cholelithiasis in 3685 post-mortem examinations performed at the Royal Melbourne Hospital during the years 1945 to 1950 was 14·9%.

2. Cholelithiasis was rare in young persons, and the frequency increased rapidly with advancing years.

3. Cholelithiasis was twice as common in females as in males. This predominance of females was greater in younger age groups, and decreased with advancing age, suggesting that parity has little influence on the development of cholelithiasis.

4. Cholelithiasis is approximately one and a half times as frequent in Australia as in England.

5. There is little knowledge of the factors responsible for these variations, but they appear to be due to both genetic and acquired influences.

Acknowledgements.

Our thanks are due to the honorary medical staff of the Royal Melbourne Hospital for permission to publish these results.

References.

BECKER, B. J. P., and CHATGIDAKIS, C. B. (1952), "Carcinoma of the Gall Bladder and Cholelithiasis on the Witwatersrand", *South African J. Clin. Sc.*, 3: 13.

BOCKUS, H. L. (1946), "Gastro-enterology", Saunders, Philadelphia and London, 3: 594.

CLELAND, J. B. (1953), "Gall-stones in Seven Thousand Post-mortem Examinations", *M. J. AUSTRALIA*, 2: 488.

COOKE, L., JONES, F. A., and KEECH, M. K. (1953), "Carcinoma of the Gall Bladder", *Lancet*, 2: 585.

CRUMP, C. (1931), "The Incidence of Gall Stones and Gall Bladder Disease", *Surg., Gynec. & Obst.*, 53: 447.

DESSAU, F. I. (1943), "The Incidence of Gall Stones in the Higher Age Groups", *New England J. Med.*, 229: 464.

ENGLISH, C. (1927), "Gall Stones", *Lancet*, 1: 1210.

GROSS, D. M. B. (1929), "A Statistical Study of Cholelithiasis", *J. Path. & Bact.*, 32: 503.

HAMILTON, I. (1932), "Gall Stones Found Post Mortem", *M. J. AUSTRALIA*, 2: 78.

HURST, A. F. (1923), "Cholelithiasis and Gall Stones in Light of Recent Research", *Practitioner*, 111: 321.

JAFFÉ, R. H. (1933), "Cholelithiasis: Statistical Study with Special Reference to its Frequency in Coloured Race", *J. Lab. & Clin. Med.*, 18: 1220.

LUDLOW, A. I. (1930), "Cholelithiasis in the Korean", *Surg., Gynec. & Obst.*, 50: 51.

LUDLOW, A. I. (1937), "Autopsy Incidence of Cholelithiasis", *Am. J. M. Sc.*, 193: 481.

MITCHELL, L. J. (1918), "Incidence of Calculi of Gall Bladder as Met With in 1600 Necropsies", *Ann. Surg.*, 68: 289.

MOSHER, C. D. (1901), Abstract: "Frequency of Gall Stones in United States", *Bull. Johns Hopkins Hosp.*, 12: 253.

POTTER, A. H. (1928), "Gall Bladder Disease in Young Subjects", *Surg., Gynec. & Obst.*, 46: 795.

RYERSON, E. S. (1911), "Ætiology of Cholelithiasis", *Canad. M. A. J.*, 1: 822; quoted by Dessau, F. I., *loco citato*.

SEIDLER, V. B., and BRAKELEY, E. (1940), "Gall Stones in Children: Report of a Case Diagnosed by Roentgen Examination and Confirmed at Operation", *J.A.M.A.*, 114: 2082.

SPENCE, G. R. (1941), "Cholelithiasis in Newborn Infants", *Arch. Pediat.*, 58: 479.

ULIN, A. W., NOSAL, J. L., and MARTIN, W. L. (1951), "Cholecystitis in Childhood: Report of a Case with Common Duct Calculi", *J.A.M.A.*, 147: 1443.

Reports of Cases.

THE IMMEDIATE ACTION OF TRIETHYLENE MELAMINE IN CHRONIC LYMPHATIC LEUCHÆMIA.

By J. H. BOLTON, M.D., M.R.C.P.,

AND

R. H. D. BEAN, M.B., B.S.,

Repatriation General Hospital, Heidelberg, Victoria.

TRIETHYLENE MELAMINE and related substances have been used to improve surface finish in the textile and paper industries for some years. In 1949, as a result of systematic investigation, TEM was discovered to be a powerful inhibitor of the growth of certain artificially induced neoplasms in animals (Rose *et alii*, 1950; Lewis and Crossley, 1950). By 1951, clinical trials of the drug were proceeding in both Great Britain and America, and the drug had shown considerable promise in the treatment of human malignant disease, particularly chronic leuchæmia and Hodgkin's disease.

There has been considerable recent speculation upon the manner of action of TEM. The drug bears a close relationship to nitrogen mustard (Figure I). The biological effect of these agents is considered to be due to the nucleotoxic activity of ethylene-imine groupings in the molecules. TEM possesses three of these groupings, while *bis* nitrogen mustard releases two upon hydrolysis.

Recent investigation into the action of this drug has been directed towards elucidating the manner of interference with chromosome reproduction, and largely carried out upon plants and experimental animals at a cellular level.

We consider that the emphasis placed on these aspects has resulted in insufficient attention being paid to certain properties such as lipoid solubility, and further investigation is required into the reaction of the biological system of man as a whole to the drug.

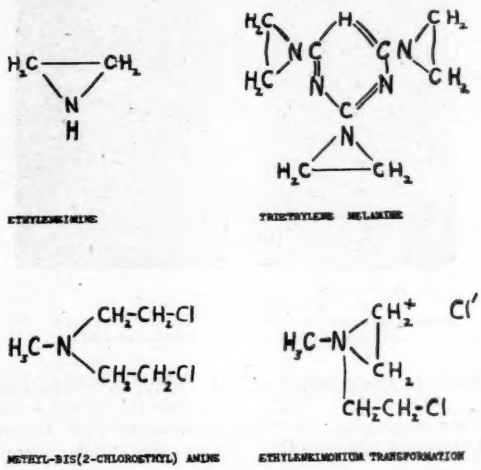

FIGURE I.
The relationship between methyl-bis-chlorethylamine (nitrogen mustard) and triethylene melamine (TEM).

In this paper the effect of TEM upon the hæmatopoietic system of three patients suffering from chronic lymphatic leuchæmia has been studied by serial examinations, consisting of daily counts of white blood cells (total and differential), red blood cells, platelets and reticulocytes. In one case the hæmoglobin and stercobilinogen excretion was also measured daily, and the bone marrow was examined at approximately weekly intervals.

Case I.

The patient was a male, aged thirty-eight years, who had been suffering from chronic lymphatic leuchæmia for at least three years prior to this study. He had been treated with TEM over a period of nine months with marked clinical and hæmatological improvement. On this occasion he was given five milligrammes of TEM on June 6 and again ten days later.

Reference to Figures IIA and IIB will show that the following fall in the total white blood cell count is describable in two phases. The first phase commenced shortly after the administration of the drug and reached a maximum in two to four days. Its characteristics are a fall in the total number of white blood cells, a fall in the number of smear cells, a rise in the number of unsmeared lymphocytes and mature neutrophile cells present, and a rise in the excretion of stercobilinogen, this last being probably significant. This phase was accompanied by a sharp increase in the size of the spleen, which reached a maximum when the total white blood cell count fell to its lowest point (Figure III). During this first phase the patient complained of lassitude, nausea and general malaise. This fall was succeeded by a gradual rise in the number of lymphocytes, smear cells and leucocytes.

The second phase is characterized by a decline in the number of neutrophile cells, lymphocytes and smear cells, which reached its lowest point in ten to fourteen days after the administration of TEM. This change was not so dramatic as the first phase, and was accompanied by clinical improvement. After this fall the count gradually rose until a further dose of TEM was administered. Figures IIA and IIB show that this sequence was repeated on each occasion when the drug was administered. Although the number of platelets and the stercobilinogen excretion were

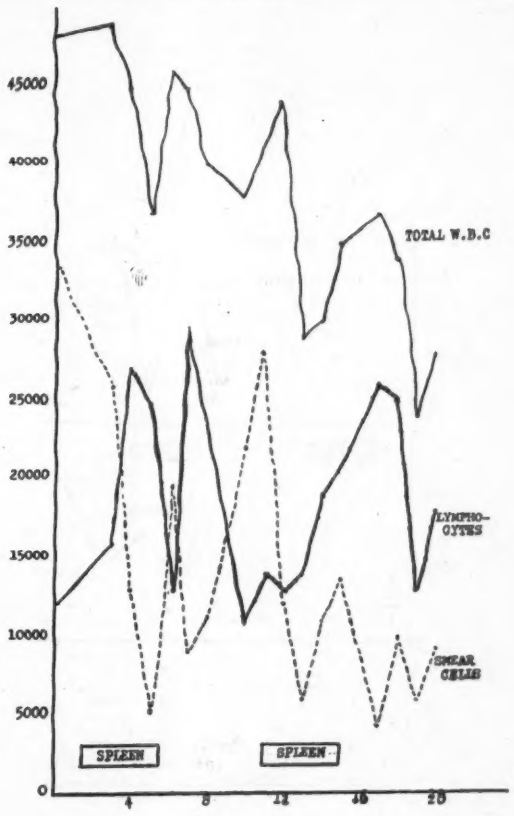

FIGURE IIA.
Changes in the blood in Case I.

measured only on the second occasion, a bone marrow examination performed during the first phase at the peak of splenic enlargement shows relative prominence of the granulocytes, which contrasts with their fall in the peripheral blood. A second examination performed during the second phase showed a diminution of myeloid activity, and a considerable decline in the number of smear cells (see accompanying myelogram, Table I).

Comment.

Close examination of the hæmatological and clinical findings in this case shows that the factor which is responsible for the greater part of the fall in the total number of white blood cells is the smear cell component. The sharp drop in the number of smear cells occurs simultaneously with a rapid increase in the size of the spleen, and this correlation suggests that this is a work hypertrophy of the spleen. Supportive evidence is provided by the fall in the number of platelets and neutrophile cells. Although the

red blood cell count shows a less pronounced change, there is an increase in total stercobilinogen excretion, which may be evidence of red blood cell destruction attributable to splenic over-activity.

The number of unsmeared white cells, both lymphocytes and granulocytes, is sharply increased. A possible explanation of the increased myeloid activity of the marrow occurring during this time is utilization of or stimulation by the products of destruction of the smear cells.

The fall in the second phase is essentially one of depression, affecting all elements of the white cell population. The accompanying myelogram shows mainly an erythroid phase, perhaps compensatory to the previous hypersplenic phase.

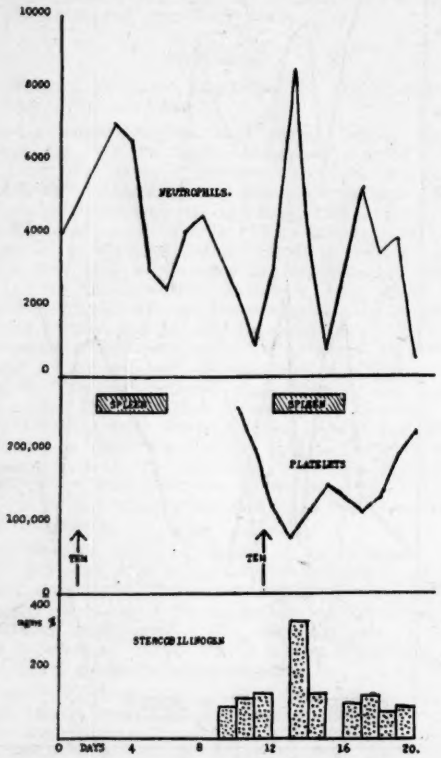

FIGURE IIB.
Blood changes and quantitative stercobilinogen excretion in Case I.

The bone marrow changes may be interpreted as showing a lag between a myeloid and an erythroid response, perhaps due to the fact that responses involving the red cell mass are generally slower than those involving the white blood cells, or that nutritional factors are differentially utilized.

Case II.

A male patient, aged sixty-four years, had been discovered to be suffering from lymphatic leuchæmia at a blood examination approximately two years previously. Over this period his clinical condition had deteriorated and his lymphocyte count had steadily risen. A distinctive feature had been the progressive decrease in the hæmoglobin value and in the number of neutrophile cells, which was regarded as evidence of bone-marrow involvement, confirmed by biopsy. Although the presence of neutropenia is a recognized contraindication to the use of TEM, Rundles and Barton (1952) consider the drug of most value in the treatment of patients with bone-marrow involvement, and it was decided to observe the effect of a dose. The patient received 12·5 milligrammes of TEM over a period of five days. Within three days of the first dose the total white blood cell count commenced to fall, and this was paralleled

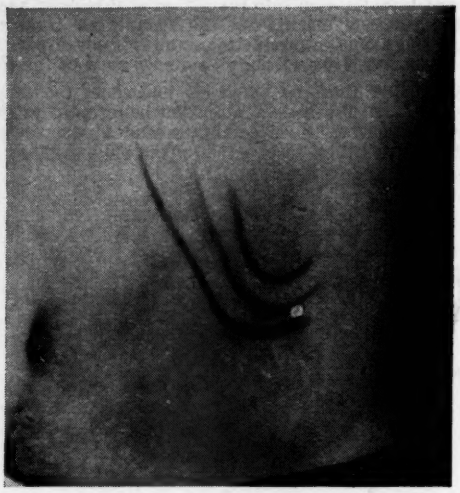

FIGURE III.
Skin marking to show progressive increase in splenic size following TEM therapy.

by a fall in the numbers of both granulocytes and lymphocytes (Figure IV). At the same time the spleen enlarged, and six days after the commencement of TEM therapy it had reached his pelvis. His lymph glands practically

TABLE I.

Type of Cell.	June 19, 1953.	June 29, 1953.
Myelocytes:		
Neutrophile cells	0·4%	1·5%
Eosinophile cells	—	0·5%
Basophile cells	—	—
Metamyelocytes:		
Young neutrophile cells	0·4%	3·0%
Eosinophile cells	0·4%	—
Old neutrophile cells	0·4%	—
Eosinophile cells	—	—
Polymorphonuclear cells:		
Neutrophile cells	12·0%	9·5%
Eosinophile cells	—	—
Basophile cells	—	—
Monocytes	—	3·0%
Lymphoblasts	1·2%	—
Large lymphocytes	1·2%	—
Lymphocytes	47·6%	57·0%
Blast cells	—	—
Plasma cells	—	—
Pronormoblasts	—	—
Normoblasts:		
Basophile cells	—	1·0%
Polychromatic cells, early	—	6·5%
Polychromatic cells, late	0·9%	1·0%
Cells in mitosis	—	0·5%
Smudge cells	35·5%	16·5%

vanished over this period. The fall in the total white cell count ceased approximately three days after the cessation of the administration of TEM, and the total white cell count then remained at a steady figure over the period of these observations.

Comment.

The differential count shows two phases, which bear a close similarity to those described in the first case, the lowest point in smear cell and lymphocyte count in this case coinciding with maximum splenic enlargement. The numbers of both lymphocytes and smear cells then commenced to rise until ten days after the cessation of TEM therapy, when a further and more gradual fall took place.

Case III.

A male patient, aged thirty-eight years, had been discovered to be suffering from chronic lymphatic leuchæmia

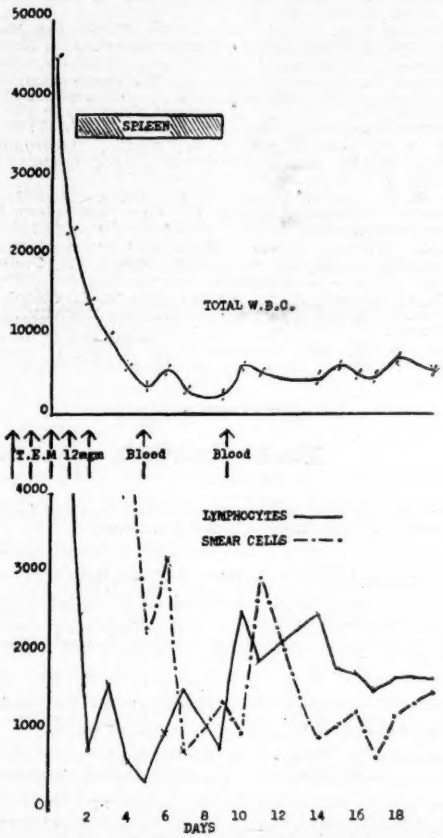

FIGURE IV.
Blood changes in Case II.

approximately three months previously. He had been given TEM on three previous occasions, with a good response on each occasion. He was given five milligrammes of TEM on June 22. The accompanying diagram shows the changes in total and differential white blood cell counts which followed (Figure V). Splenic enlargement commenced within twenty-four hours of the administration of the drug and remained for seven days. The accompanying diagram (Figure IV) clearly shows that this phase of splenic enlargement is paralleled by the fall in the number of smear cells, which appear to be the elements most readily affected by splenic over-activity.

Comment.

This case shows features similar to those in the previous cases. There is an immediate fall in the total number of white blood cells, which occurs simultaneously with an increase in splenic size. Two other features worth noting are the presence of the double peak in both smear cells and lymphocytes, and the reciprocity between these cells, which in this case conceals the second peak in the total cell count.

Discussion.

The important observation in these cases is the coincidental initial fall in the number of white blood cells and the sharp increase in the size of the spleen. These two occurrences must be closely related.

Examination of the current literature shows that these observations have been substantiated by other workers in both the clinical and the experimental fields.

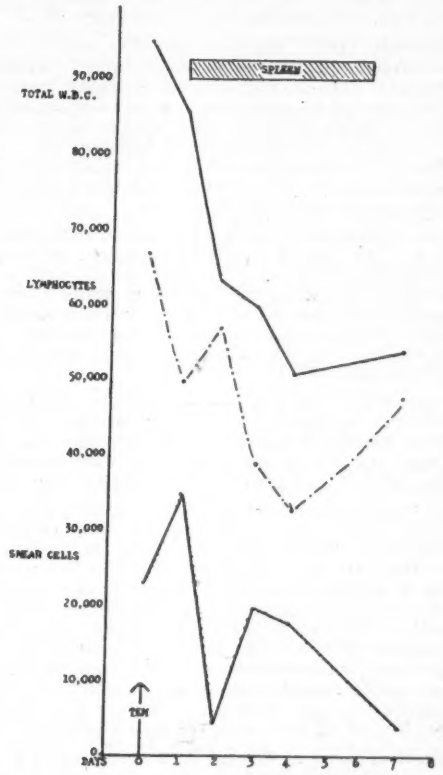

FIGURE V.
Blood changes in Case III.

A significant recent paper, published after the foregoing observations were made, is by Crossley and others (1953), who have reported a series of experiments upon the distribution of P^{32} labelled triethylene phosphoramide in rats. This drug is not only structurally related to TEM, but also shows an identical cytotoxic action. These observers have noted a gradual accumulation of P^{32} in the spleen over a period of thirty hours after the administration of the drug. This work substantiates our clinical findings.

There appear two explanations for these phenomena: firstly, that TEM directly stimulates the phagocytic activity of reticulo-endothelial tissue, the destruction of blood cells then being secondary to this stimulation, and secondly, that TEM damages certain blood cells in such a manner as to increase their liability to phagocytosis, and the increase in splenic size is then a work hypertrophy.

Crossley *et alii* in their paper support the postulation of reticulo-endothelial stimulation. We consider that there are reasons for believing that this is not the more likely possibility. Observations in other reticuloses, not recorded

in this paper, have shown that the hypersplenic effect is not so pronounced as in chronic lymphatic leuchæmia. In this latter condition there is a considerable increase in the number of circulating abnormal cells, destruction of which appears to enhance the hypersplenic effect. Thus the magnitude of the hypersplenic effect is more closely related to the number of cells destroyed than to the dose of the drug. Again, the gradual accumulation of P^{32} over a thirty-hour period as described by Crossley is suggestive of an indirect effect.

We consider that the bulk of the evidence favours the second postulation, and that the properties of the drug are important in this regard. These agents in their unreacted state are lipoid-soluble. Kinsey and Grant (1947) have shown that in yeast cells 40% of nitrogen mustard remains with the lipoid framework after extraction.

Friedenwald (1951) has remarked that such concentrations of nitrogen mustard might be expected to damage the cell structure. Smear cells are mechanically fragile and would be expected to show the most pronounced effect of this attack. These cells are most readily phagocytosized by the spleen. This destruction is apparent both in the reduction in the blood count in our cases and in the accumulation of P^{32}. Platelets and red blood cells do not escape the hypersplenic effect.

It does not appear reasonable to attribute this first change to bone-marrow depression, because of both the short time interval between the administration of the drug and the observed fall in the number of white blood cells, and the fact that the fall affects only certain elements of the blood. Further evidence against bone-marrow depression is provided by the biopsy in Case I, which showed quite pronounced activity.

On the other hand, it would appear reasonable to attribute the secondary fall to bone-marrow depression, because it affects all the white cell elements, and in all three cases the size of the spleen had become reduced to less than what it was prior to the administration of TEM.

What are the reasons for these phenomena? The current view that TEM acts by interference with chromosome reproduction is not adequate to explain all these observations. Danielli, as a result of experiments on nuclear transfer in amœbæ, has uttered a warning against attributing too much importance to nuclear changes which are non-specific and are detected by staining reactions. It would appear from the observations of Crossley *et alii* and ourselves that this rather mechanistic view of the action of these agents requires modification, and in any case the reactions of the body as a whole, rather than those of a series of individual cells, have not been studied sufficiently.

A practical point in therapy with this drug is that this phase should be recognized as largely hypersplenic, and the fall in the number of white blood cells not attributed to damage to the bone marrow. Incorrect interpretation of this may be regarded as a contraindication to TEM, and the use of a valuable agent may be abandoned.

Summary.

1. The hæmatological and clinical changes immediately following TEM therapy in three patients suffering from chronic lymphatic leuchæmia are described.

2. Evidence is presented to show that the following fall in the number of white blood cells occurs in two phases. The early phase occurs within one to seven days of the administration of TEM, and its main characteristics are a sharp fall in smear cells and some other formed elements of the blood, probably attributable to hypersplenism. The fall in the late phase is probably evidence of bone-marrow depression.

3. The hypersplenic phase is attributed to work hypertrophy following damage to cell structures by TEM.

4. The importance of distinguishing the hypersplenic phase and differentiating this from bone-marrow depression is emphasized.

Acknowledgement.

We desire to thank Dr. J. W. Bennett, of the Repatriation General Hospital, Heidelberg, for his observations in the second case, and the staff of the Royal Melbourne Hospital for their observations in the third case. We acknowledge our indebtedness to the pathology department for their assistance in these investigations, and are grateful to the Repatriation Commissioner for permission to publish this material.

References.

CROSSLEY, M. L., ALLISON, J. B., WANNEMACHER, R., MIGLIARESE, J., PARKER, R. P., KUR, E., SEEGER, D. R., and PARTRIDGE, R. (1953), "Distribution of P^{32} Following Injection of TEPA in Rats", *Proc. Soc. Exper. Biol. & Med.*, 83: 398.

DANIELLI, J. F. (1952), "Cytochemical and Cytological Studies of Drug Action", *Nature*, 170: 863.

FRIEDENWALD, J. S. (1951), "The Action of Nitrogen Mustards and Related Substances on Cell Division", *Ann. New York Acad. Sc.*, 51: 1432.

KARNOFSKY, D. A., BURCHENAL, J. H., ARMISTEAD, H. C., SOUTHAM, C. M., BERNSTEIN, J. L., CRAVEN, L. F., and RHOADS, C. P. (1951), "Triethylene Melamine in the Treatment of Neoplastic Disease", *Arch. Int. Med.*, 87: 477.

KINSEY, J. E., and GRANT, W. M. (1947), "Distribution of Fixed Mustard Gas in Yeast", *J. Cell & Comp. Physiol.*, 29: 51.

LEWIS, M. R., and CROSSLEY, M. L. (1950), "Retardation of Tumour Growth in Mice by Oral Administration of Ethylenimine Derivatives", *Arch. Biochem.*, 26: 319.

PATERSON, E., and BOLAND, J. (1950), "Trisethyleniminos-triazine in Human Malignant Disease. A Preliminary Trial", *Brit. J. Cancer*, 5: 28.

ROSE, F. L., HENDRY, J. A., and WALPOLE, A. L. (1950), "New Cytotoxic Agents with Tumour Inhibitory Activity", *Nature*, 165: 993.

RUNDLES, R. W., and BARTON, W. B. (1952), "Tri-ethylene Melamine in the Treatment of Neoplastic Disease", *Blood*, 7: 483.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Textbook of Operative Gynæcology", by Wilfred Shaw, M.A. (Camb.), M.D., F.R.C.S. (England), F.R.C.O.G.; 1954. Edinburgh and London: E. and S. Livingstone, Limited. 11½" × 9", pp. 454, with 382 illustrations. Price: £5.

The author has described the surgical methods adopted by himself.

"Pomp and Pestilence: Infectious Disease. Its Origins and Conquest", by Ronald Hare, M.D.; 1954. London: Victor Gollancz, Limited. 8" × 5½", pp. 224. Price: 12s. 6d.

The author is Professor of Bacteriology in the University of London at St. Thomas's Hospital Medical School.

"Medical Mycology", edited by R. D. G. Ph. Simons; 1954. Amsterdam: Elsevier Publishing Company. 9" × 6½", pp. 460, with 342 illustrations, a few in colour. Price: 55s.

Comprises 41 chapters by thirty-six contributors.

"Beyond the Germ Theory: The Roles of Deprivation and Stress in Health and Disease", edited by Iago Galdston, M.D.; 1954. New York: The New York Academy of Medicine, published by the Health Education Council. 8½" × 5½", pp. 190, with 15 text figures. Price: $4.00.

An extension of the material presented at the annual Eastern States Health Education Conference sponsored by the New York Academy of Medicine.

"William Clift", by Jessie Dobson, B.A., M.Sc.; 1954. London: William Heinemann (Medical Books), Limited. 9" × 6", pp. 152, with 32 illustrations. Price: 21s.

William Clift was the first conservator of the Hunterian Museum of the Royal College of Surgeons of England.

"Having a Baby", by J. F. Robinson, M.B., Ch.B.; 1954. Edinburgh and London: E. and S. Livingstone, Limited. 7½" × 5", pp. 100, with 23 text figures. Price: 6s. 6d.

Intended for young married couples.

The Medical Journal of Australia

SATURDAY, SEPTEMBER 18, 1954.

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ALMROTH WRIGHT.

THE injunction in Ecclesiasticus, "Let us now praise famous men", is too often forgotten. When the leaders of the medical profession die, obituary notices are published about them in medical journals and their works are extolled, their characters are described, and generally word pictures are painted of them as individuals. Later on, biographies may appear, and these reach a wider circle of readers than the notices which have appeared in scientific journals. We may say that in these ways famous men are praised, and it is well that it should be so. Those who have to follow in the paths trodden, or maybe opened up, by leaders in medicine may be stimulated and encouraged by biographies; they may merely be entertained, but they may also, if they are men of discernment, be warned. When Almroth Wright died on April 13, 1947, he was acclaimed as a leader in medicine—one of what have been called the "pathfinders in medicine". It is true that there were many of his day and generation who would accept only some of his teaching and who were prepared to find fault with him on many occasions; but no one can deny that he had epoch-making achievements to his credit and that he provoked thought among those who were capable of serious thinking. The present reference to him is occasioned by the publication of a book in which he is described as a "Provocative Doctor and Thinker".[1] The book is by Dr. Leonard Colebrook, F.R.S., who worked with him for many years and who writes as a pupil of a revered master, with enthusiasm, but as far as can be determined, with wise judgement.

[1] "Almroth Wright: Provocative Doctor and Thinker", by Leonard Colebrook, F.R.S.; 1954. London: William Heinemann (Medical Books), Limited. 9" x 5½", pp. 298, with 288 illustrations. Price: 21s.

We may observe at once that Colebrook ranks Almroth Wright among the great pioneers, in the company of Claude Bernard, Pasteur, Koch, Metchnikoff and Ehrlich. Wright studied art and medicine at Dublin. He took his Arts degree with first class honours and a gold medal in 1882, and in the following year graduated in medicine. He was awarded a medical travelling prize and for a while read jurisprudence and Roman and international law at Inns of Court. He became a demonstrator of pathology at the University of Cambridge in 1887 after having studied at several universities in Germany. He took his M.D. in Dublin in 1889, and soon after that became demonstrator in physiology at the University of Sydney. It is strange that at Sydney he seems to have created no impression at all—there is no legend about him as there has been about some other famous people who have served at the Sydney medical school. As a matter of fact, Wright had a great deal of trouble before he found his true niche. When he became Professor of Pathology at the Army Medical School at Netley, he certainly appeared to have created an impression, for in 1906, at the summer festival, he was given the honorary degree of Doctor of Science at his old University. In the Latin presentation speech before the conferring of the degree, the following words were used (the translation is given by Colebrook): "The fire of his genius has drawn him pupils from other occupations, and excited them with such keenness, such capacity for work, such emulation in the pursuit of truth, that his school has sent forth, like the Trojan horse, none but masters among men." It should, perhaps, be pointed out that Wright had some hesitation in taking up a medical career, for he had a double qualification—modern literatre and medicine. He was not the only prominent worker in medicine who has been thus equipped. When Wright sought the advice of Professor Edward Dowden, Professor of Literature, Dowden gave him Lamb's advice: "Literature is a good stick but a poor crutch." Colebrook does not think that Wright seriously considered the claim of literature rather than medicine. However, he did spend a large part of his life in writing, and was once told by Bernard Shaw: "You can handle a pen as well as I." Colebrook points out that for nearly nine years after he graduated in medicine Wright had no contact with practical doctoring; probably he never entered a hospital. He had, however, caught glimpses of the new world of medical science in the laboratories of such men as Ludwig and Cohnheim, of Weigert, Goltz, Hoppe-Seyler and Kulz, of Victor Horsley and Woolridge, of Roy and Gaskell and of Michael Foster. He was training himself "to look beneath the surface of things" and "to proceed from the known to the unknown". It was when he was offered and accepted the chair of pathology at Netley that he found his true sphere. Wright had round him at Netley a group of men only a few years younger than himself who were eager to join him in his quest for new knowledge. He introduced them to a world of new ideas, to a medicine in which measurement and experiment were to play an ever-increasing part, a medicine requiring at every stage new apparatus and technique, which he encouraged them to devise for themselves. Wright was a past-master at the devising of apparatus, and much of the apparatus he fashioned was extremely simple. This was the subject of comment by Sir Henry Dale at the

opening of the new institute at St. Mary's Hospital in 1936. Dale used the following words: "I sometimes think that we might regard Sir Almroth Wright as one of the born burglars of Nature's mysteries, fashioning his skeleton keys with his own ingenious fingers from the most homely materials, and using them with a touch of genius to force one after another of the intricate locks with which Nature seems to guard her secrets." Colebrook's account of Wright's struggle to secure the adoption of antityphoid inoculation is one of the most interesting parts of his book. Wright was an Irishman, and Irishmen know how to fight. Shortly after Wright's first paper on this subject appeared in 1897, typhoid fever broke out in an asylum housing 1650 patients in Kent. In response to a request for help, Wright inoculated 84 members of the staff who volunteered for the trial; 118 were not inoculated. Among the 84 inoculated persons there were no cases of typhoid fever; among the uninoculated there were four. This was a satisfactory beginning. The South African War gave a wonderful opportunity for the trial of antityphoid inoculation, but it was allowed to be carried out only on men who voluntarily presented themselves to have it done. Only some 14,628 men volunteered for it out of a total of 328,244 (about 4%). It was extremely difficult to follow up the 14,000 men inoculated, and very often when a man was asked if he had been inoculated, he said that he had in order to avoid inoculation. Again, some non-commissioned officers scored men up as having been inoculated because it stood to reason that if they got typhoid fever "they must have been inoculated". A fierce controversy took place and one of Wright's chief opponents was Professor Karl Pearson, who attacked the subject from the statistical point of view. In the long run Wright prevailed, and we read that if Pearson had had his way, or if Wright had not fought strenuously for the application of antityphoid inoculation to the army, the immense benefits of that procedure would have been postponed for many years and would probably not have been available for the 1914-1918 war.

As would be expected, Colebrook writes a great deal about Almroth Wright's conception of the opsonic power of the blood. Wright's own work on antityphoid immunization and Pasteur's earlier work on anthrax, chicken cholera and rabies made it clear that there were in the animal and human body great forces lying latent which could be called into action by appropriate stimuli. Wright set to work to find how these stimuli should be applied. He saw in Metchnikoff's work on phagocytosis the clue that he was seeking. He wished to be able to discover when a patient had responded to an inoculation against a microbic infection if the clinical condition showed no dramatic change. Metchnikoff's observations had been made on the phagocytes of larval starfishes into whose tissues he had inserted tiny splinters of wood. Wright saw in phagocytosis a probable mechanism in the recovery from microbic diseases. He thought that it might be possible by appropriate methods to find out whether the phagocytes of a man suffering from boils were more or less active than those of a normal man, whether they could be stimulated to greater activity by means of an inoculation of vaccine, and how long the effect of such a stimulation would last. In other words, he thought that the study of phagocytosis might furnish a clue to the body's immunity or "resistance" to a particular microbe, and to the variations of that immunity from time to time. Wright was joined in this work by S. R. Douglas, and they soon found that the disposal of microbes by phagocytes in the body was not so simple as Metchnikoff had supposed. It was not enough for the phagocytes and the microbes simply to come together—the latter had to be "prepared" in some way before they would be engulfed and digested. This was brought about, it seemed, by some property of the blood serum, a property to which Wright gave the name "opsonic". Colebrook describes this as a fundamental discovery of the first importance, possibly the most far-reaching since Pasteur's discovery that fermentation was due to bacterial action. He thinks that it was important in three ways. First of all, it clarified the views held as to the mechanism of recovery from microbial diseases. There had been a sharp divergence of viewpoints on this matter. According to one school, the microbes were destroyed (or their poisons neutralized) by the blood fluids. According to the other school, the phagocytes were the essential factor behind all immunity processes. The work of Wright and Douglas "married" these two conceptions and showed that both mechanisms played important roles; in some diseases the former were more important, in other diseases the latter. Secondly, it was important because it gave a new precision method for the diagnosis of at least some microbic diseases. Thirdly, Wright's conception opened up a big new field for exploration in the treatment of microbic diseases. The temptation to enlarge further on Wright's ideas about opsonins and the opsonic index must be resisted for lack of space. It should be noted, however, that Colebrook sets out in a chapter entitled "Wright's Creed" no less than nineteen items which Wright proclaimed at different stages of his work. Colebrook points out that of the nineteen items in this creed, no less than ten have been "passed up" and are not commonly handed on to students. One of the ten items in this creed was that the functional activity of leucocytes does not vary in health and disease. This was shown to be untrue by Shattuck and Dudgeon in 1908, and it is important to note that Wright himself acknowledged his mistake. That a worker of Wright's calibre should acknowledge his mistake is to his credit and should be remembered by those who do not regard him as highly as Colebrook does. Colebrook states that the other nine which are not at present handed on to students may have been unworthy to survive because they were erroneous, but he adds that this should not be assumed. He thinks that the non-acceptance of some of these items must be traced to the fact that during Wright's latter years there developed a "climate of opinion" which was unfavourable or just indifferent to his views. Three circumstances are named as having contributed to this unfavourable climate of opinion. The first was that Wright's forceful personality and dialectical combativeness inevitably aroused some personal antagonism. The second was that there were many for whom Wright's doctrines for one reason or another were uncongenial. The third was that there were not lacking critics of the financial arrangement by which the St. Mary's laboratory was equipped and maintained. Colebrook, who worked with Wright on phagocytosis,

writes in one place that "looking back, and being wise after the event, one cannot but regret that we attempted so much. We might have won more solid scientific gains if we had made haste more slowly". For all this, Colebrook's judgement is that no one except Pasteur (and perhaps Ehrlich) did more in the past century to "build up in the human understanding a true model of the world (of immunology) as it is in fact", and to bring bacteriology to the service of medicine. Colebrook heads one chapter "Pain in the Mind". He says that the phrase has been attributed to Abraham Lincoln, but adds that Wright was never without that pain—it was a continual spur to him. Reading this book, which it must be confessed holds the reader's interest to a remarkable degree, one can well believe that this is true of Wright. In one place we have a quotation from Emerson: "God offers to every mind its choice between truth and repose." The whole history of Wright's work shows that he seldom had repose. He was always searching for something new, always worried by the ills of humanity, by the inability of medicine to cope with the tremendous problems which had to be faced, and by the inadequacy of efforts that he and others could make. He was certainly one of the most remarkable and versatile men of the modern age. Nothing has been written here of Wright's association with Bernard Shaw or of his strong opposition to the cause of woman's suffrage. A leading article in *The Lancet* of May 10, 1947, concludes as follows:

> Always an uncompromising individualist, Wright seemed to take little notice of what other people found out. Nor did he make much attempt to fit his observations into the corpus of accumulated knowledge. Nevertheless he took immense pains over exposition, and in his belief that language could be made a better vehicle of thought he invented a number of new words, some of which will survive. He had a great dislike of statistics, and was in many other ways wilful and wayward. Some thought of him as a hero; others as a grim lion, liable at any moment to turn and rend; others again as just a wrong-headed rebel. But none can now deny him the salutary influence of the original mind which invades the holy places of accepted dogma and sets up signposts in deserts. Often these signs have led us otherwhere than he or we expected, but they have kept us on the march.

Bernard Shaw, writing in the *British Medical Journal* after Wright's death, stated that men of science are usually rich in facts and poor in logic. The *British Medical Journal* declares that Shaw's friend, Almroth Wright, was rich in both.

Current Comment.

CORTISONE AND ACTH IN DERMATOLOGY.

CORTISONE AND ACTH exert a powerful influence on many skin diseases, but this does not imply that they are the best form of treatment or that their use in this field is justified at all. Generally speaking, according to F. F. Hellier,[1] they have no action on the skin when used locally. On the other hand, hydrocortisone (compound F) has a marked effect on the skin. Skin conditions for which general treatment with cortisone and ACTH may be used are roughly divided by Hellier into four groups: (i) fatal and severely incapacitating skin conditions for which cortisone and ACTH may be the only life-saving or controlling treatment available (these include pemphigus, acute *lupus erythematosus*, generalized exfoliative dermatitis and *polyarteritis nodosa*); (ii) severe self-limiting conditions in which cortisone and ACTH produce marked improvement and may greatly diminish the patient's suffering and period of illness, and even avert serious complications; (iii) chronic non-fatal skin diseases which can be controlled by cortisone or ACTH; (iv) chronic serious dermatoses for which cortisone and ACTH are of little value. Pemphigus can be controlled in many cases for prolonged periods with cortisone or ACTH. The beneficial effect is observed only while the drug is being given, and soon after its administration is stopped the patient usually relapses. It is necessary to keep the patients on a maintenance dose, and with this they have been kept well for over two years. Acute *lupus erythematosus* can be dramatically alleviated. But despite this, the laboratory findings are little altered; the blood sedimentation rate remains high, and L.E. cells are still found in the blood. Some patients require as much as 100 milligrammes daily to control the disease. Once the acute phase has settled, a much smaller maintenance dose may control the acute stage, possibly about 100 milligrammes or even less daily. Despite treatment, many patients die. *Polyarteritis nodosa* is usually a fatal disease, but responds to cortisone and ACTH in a way similar to acute *lupus erythematosus*. Generalized exfoliative dermatitis, when due to a toxic action of gold, bismuth or arsenic, may respond dramatically with the use of cortisone. Exfoliative dermatitis may appear spontaneously (the idiopathic variety). There may be much enlargement of the lymphatic glands, which show deposits of lipoid and melanin. Administration of cortisone produces a rapid improvement in these cases. A permanent dose of 100 milligrammes daily may be necessary as a maintenance dose to keep the patient from relapsing. Severe drug reactions, both eczematous and urticarial, may be more quickly relieved by treatment with cortisone than by any other method. Severe types of *erythema multiforme*, the so-called Stevens-Johnson syndrome, are more speedily relieved by cortisone than by "Aureomycin". It is debatable whether the use of cortisone is justified in such conditions as chronic eczema and psoriasis. *Lichen planus* of the widespread variety will often fade dramatically with a short course of cortisone. It can cause rapid alleviation of acute urticaria, but is unfortunately of little value for chronic urticaria. In the treatment of *alopecia totalis* it should be considered, but the condition relapses on ceasing administration of the drug. Hellier has had one dramatic cure with its use in the treatment of *pityriasis rubra pilaris*. Unfortunately, cortisone and ACTH have been found to have no effect on the real course of such diseases as *mycosis fungoides*, Hodgkin's disease and leuchæmia, and their use in all tuberculous conditions is definitely contraindicated.

The dose varies with the individual. It is usual to start with 100 to 200 milligrammes of cortisone or 50 to 100 milligrammes of ACTH divided into four doses a day. Once a good response is obtained, the dose should be lowered until the maintenance level is determined. This is often in the region of 75 to 100 milligrammes of cortisone. After a course of cortisone the activity of the adrenal gland may be decreased, and it is possibly wiser to change to ACTH, which can then be gradually tailed off. Toxic symptoms should be watched for. The blood pressure may be raised and a mild degree of Cushing's syndrome develop. Symptoms of infection may be suppressed, with masking of such conditions as pneumonia. The patient must be thoroughly examined to exclude tuberculosis, *diabetes mellitus* and marked hypertension, and it must be borne in mind that retention of salt and fluid and other changes may occur, leading to œdema, increase of weight and possibly serious cardiac upsets from loss of potassium.

Hellier's review brings out most of the significant points for and against the use of cortisone and ACTH in dermatological therapy. It is apparent that the position is much the same now as it was in 1951, when M. B. Sulzberger, V. H. Witten and S. N. Taffe[1] described the "effectiveness of this new therapeutic approach" in a wide variety of skin diseases and agreed that "no other modality" known to them had had comparable beneficial

[1] *Practitioner*, May, 1954.

[1] *Arch. Dermat. & Syph.*, November, 1951.

effects. At the same time, they stressed the fact that the benefits generally ceased soon after cortisone therapy was discontinued, unless the disease or the attack was one with spontaneous remissions. They found that disagreeable and sometimes dangerous effects still precluded the use of this treatment except for serious diseases and in serious situations, and certainly unless the patient could be kept under sufficiently close and expert surveillance.

COLIC IN INFANTS.

MOST of us are familiar with the infant who, for a reason that is difficult to find, screams in the evening. And many a mother and many a father has been distracted by it. The baby seems healthy, is gaining weight well and seems to be having a perfectly satisfactory feeding, but yet in the evening it has what appear to be rhythmical bouts of pain that cause it to scream and not be comforted. During attacks unduly loud borborygmi can often be heard in the baby's abdomen. The complaint is commonly called colic, or three months' colic, because by the age of three months most babies have ceased to be affected by it.

R. S. Illingworth, a patient, meticulous and critical observer of the well baby, has made a study of the possible causes of this condition.[1] He reviews the literature and discusses some of the many varied factors blamed by previous workers. These include over-feeding, underfeeding, feedings too frequent or too infrequent, feedings too rich, too weak, too hot, too cold, or containing too much fat, too much protein or too much carbohydrate. Allergy has often been blamed, and so has "hypertonicity" and over-alertness. Parents have received their share of blame for picking the baby up too much, bouncing him too much or communicating their anxiety to him. Some have claimed that the condition never occurred in hospital. Most workers claimed there was excessive wind in the bowel, but Jorup in 1952 by careful radiological studies failed to show this excessive gas; he was impressed by excessive propulsive activity of the colon and vigorous expulsion of barium given as an enema. These are but some of the causes Illingworth found in the literature, and suggested treatments are just as numerous.

Illingworth studied fifty consecutive infants with this complaint in his follow-up clinic for well babies. Whenever he saw such a baby he used as a control the next baby seen as long as it was free from any suggestion of colic. In two-thirds of the affected babies the colic began while they were still in hospital. In most of the others it had commenced by the age of fifteen days. The average age at which the colic ceased was twelve weeks, and the latest sixteen weeks. Radiological examination of seven colic babies during severe attacks failed to show excessive gas in the bowel. Illingworth found that there was no evidence that under-feeding or over-feeding was the cause. He admits that under-feeding often causes crying in the evening, but crying that is different from the rhythmic screaming of pain in the colicky baby, unrelieved by picking up or feeding. Allergy was even more common in the control group and more of this group developed eczema. No evidence of hypertonia was found, nor any difference in type of baby or parent. Spoiling was not the cause of the colic, but there was a possibility that spoiling could result from it, a suggestion emphasized by Spock. Many babies obtained some relief from sucking, and so a dummy has been the treatment recommended by some writers. While there was no evidence of excessive wind in the bowel, borborygmi were excessive in many babies during attacks, and many attacks were relieved by the passage of flatus or by an enema. Some factor other than the presence of gas seems important, and Illingworth suggests that it is of the nature of spasmodic contraction or kinking of the bowel causing a temporary localized obstruction to the passage of gas. This explanation alone accounts for the excessive borborygmi, the relief by the passage of flatus or a stool or by an enema, together with the absence of radiological evidence of an excess of air in the bowel. He is carrying out further studies by radiology and by the use of antispasmodics. He can suggest no reason why attacks should be limited to the evening. But is it surprising that a functional disturbance should come at the end of a day? It is a disturbance in a young infant who is learning a new way of life. To him the experiences and stimulations of the day are new. Strange things are not accepted by our bodies without effort. By the evening they have built up enough to disturb him. And perhaps because one of these new experiences is alimentary feeding, the disturbance expresses itself in his bowel. By the age of three months he has become more accustomed to them; adaptation has occurred. They have ceased to be a stress, and his colic has ended. We look forward to Illingworth's further studies of this perplexing problem.

[1] *Arch. Dis. Childhood*, June, 1954.

METASTATIC CALCIFICATION AND NEPHROCALCINOSIS.

THE deposition of calcium in abnormal sites, that is, in tissues other than bone, has been known for a long time, but interest has been revived by recent publications of descriptions of cases of metastatic calcification related to excessive ingestion of alkali and milk and/or calcium by patients with gastric ulcers. Metastatic calcification may have many causes in addition to excessive alkali and calcium ingestion. Thus it may occur in the administration of excessive amounts of vitamin *D*, hyperparathyroidism, chronic renal disease in young persons, complete immobilization of patients with fractures and chronic lower nephron nephrosis. Usually hypercalcæmia is found, but not always. In the nephritic types there is usually hypocalcæmia.

Isidore Snapper, W. G. Bradley and V. E. Wilson describe two cases occurring after a Sippe diet of long duration.[1] Several papers have been published on the production of calcium-rich renal stones and metastatic deposits of calcium in rats and mice fed with large amounts of calcium carbonate or an alkaline diet. Both patients had taken large amounts of "Alka-Seltzer"; whereas one had also a very high daily ingestion of calcium, the other patient took less than the recommended daily allowance. The first patient had, for fifteen months prior to admission to hospital, generalized bone and joint pains which finally became unbearable. Painless masses had developed in the left index finger, the area of the left radius and the area of the right olecranon. Radiological examination showed nodular infiltration throughout both lungs and widespread nephrocalcinosis. The blood calcium content was only 9·3 milligrammes per 100 millilitres. The patient died with uræmia. Widespread calcinosis was found with calcification of arteries. The second patient had a meat-free alkaline ash type of diet whose nature is not given and consumed large amounts of "Alka-Seltzer" over a period of eight years. She had a serum calcium content of 10·3 milligrammes per 100 millilitres on admission to hospital. Radiological examination revealed metastatic calcification involving both kidneys, the aorta and its branches and both femoral arteries together with subcutaneous calcifications in various parts of the body. Five other cases are mentioned in which the patients with ulcers of the stomach had been on a Sippe diet and showed hypercalcæmia. In these cases the blood calcium level returned to normal after milk was withdrawn from the diet.

Calcinosis of the kidney parenchyma is one of the major factors in the causation of uræmia in this syndrome. In those patients who take excessive amounts of milk, calcium and alkali, the calcium deposits are much more extensive than in the patients who have hypercalcæmia due to hyperparathyroidism and the danger of impairment of renal function is greater. M. Dworetzky describes[2] a case of what he calls milk drinker's syndrome in which the calcium deposits disappeared after cessation of milk

[1] *Arch. Int. Med.*, June, 1954.
[2] *J.A.M.A.*, June 26, 1954.

intake and the substitution of alkali powders by aluminium hydroxide gel. This patient, with a duodenal ulcer, consumed six to eight quarts of milk per day and 12 to 20 doses of alkali powder a day over a long period. He showed similar symptoms to the patients mentioned above together with extensive calcium deposits. A few months after milk was omitted from the diet and alkali was replaced by aluminium hydroxide the pains began to become less and the calcified masses to disappear. Two years later the deposits around the joints had been reabsorbed. Calcification of the aorta and common iliac arteries did not disappear and the renal condition was unimproved.

F. B. Walsh and R. G. Murray have described metastatic calcification of the conjunctiva and cornea as an early sign of hypercalcæmia.[1] The changes in the cornea are more specific than those in the conjunctiva and consist of incomplete bands of calcification. The authors of the two previous papers describe similar changes in the cornea without, however, specifying that they are part of the syndrome.

TREATMENT OF LUPUS ERYTHEMATOSUS.

RECENT reports on the effectiveness of mepacrine (quinacrine, "Atebrin") in the treatment of chronic cutaneous *lupus erythematosus* have been encouraging. In a reference to this in these columns[2] a short time ago it was stated that there seemed to be general agreement that mepacrine was effective in the treatment of chronic discoid *lupus erythematosus*, though experience with its use in the systemic form of the disease had been less satisfactory. In retrospect, according to D. M. Pilsbury and C. Jacobson,[3] there is a good deal of evidence that various compounds with chemical similarity to mepacrine have been of moderate value in the treatment of chronic cutaneous *lupus erythematosus* and to a less extent of acute visceral *lupus erythematosus*. Of these, quinine has long been used. In 1928 Martenstein treated discoid and subacute *lupus erythematosus* in 28 cases with pamaquin ("Plasmochin"), which is similar to quinine in that both are substituted 8-amino quinolines. Mepacrine, which differs from pamaquin only in the addition of a benzyl chloride group, was used for the treatment of *lupus erythematosus* by Prokoptchuk in 1940. Page in 1951 reported his independent observation that mepacrine was very effective in the treatment of discoid cutaneous *lupus erythematosus* and to a less extent of acute visceral *lupus erythematosus*. The most rapid improvement occurred in relation to acute inflamed lesions. Toxicity studies on humans with mepacrine reveal mild transient gastro-intestinal disturbances, headache, depression, and in some cases, lichenoid dermatitis and hepatitis. A case of fatal aplastic anæmia after the administration of mepacrine for *lupus erythematosus* has recently been recorded. The chief drawbacks to the clinical use of mepacrine are the disfiguring yellow discoloration of the skin and the toxic reactions which may occur after prolonged administration. In an attempt to find a chemical analogue with an action similar to mepacrine that might be less toxic and that would not colour the skin, studies were reviewed which had been carried out under the guidance of the Board of Coordination of Malarial Studies. Particular attention was paid to the effects of chloroquine. Pilsbury and Jacobson state that it appears to be useful in the treatment of discoid cutaneous *lupus erythematosus* and polymorphous light eruptions, and that their results with it warrant further investigation. Extensive studies of the chronic effect of chloroquine have been carried out on human subjects at Stateville Penitentiary. One group of 20 volunteers took 0·3 gramme of chloroquine base daily for seventy-seven days and then 0·5 gramme weekly for one year. No gross incapacity was experienced. With this information as a basis, the treatment of chronic and subacute cutaneous *lupus erythematosis* was undertaken. In 16 cases of chronic discoid *lupus erythematosus* treated with chloroquine diphosphate in daily doses of 0·25 to 0·5 gramme clinical effects were generally very good, being equal or superior to those obtained with mepacrine. During a period of observation of from four to ten months after the initiation of chloroquine therapy, no significant toxic effects were noted. In particular, the absence of pigmentation is regarded as a great boon. It seems probable that the effects of chloroquine on the skin lesions of discoid *lupus erythematosus* are suppressant rather than curative, though there is hope that permanent remission may sometimes be accomplished. Further experience will make the position clearer.

[1] *Am. J. Ophth.*, December, 1953.
[2] M. J. AUSTRALIA, July 3, 1954.
[3] *J.A.M.A.*, April 17, 1954.

POST-OPERATIVE URINARY INCONTINENCE.

THE current conception is that the striated musculature surrounding the urethra, as it lies within the limits of the two layers of the triangular ligament, constitutes the external urethral sphincter. Injury to this muscle is commonly regarded as the factor responsible for urinary incontinence after operations in this region. In contrast to this concept, according to J. E. Elliot,[1] there is good reason to believe, and much evidence to support this belief, that physiological continence of urine is primarily an unconscious or involuntary act dependent on the activity of smooth muscle about the urethra, and that the striated muscle is only an accessory. The basis for this new concept is contained in observations on the nature of micturition in normal individuals and in those with disease of the spinal cord; on certain anatomical relationships of the male urethra; and on observations of patients who have undergone prostatectomy. Most individuals are unaware of their bladder until it contains 250 cubic centimetres or more of urine. During the period of filling no effort is required to maintain continence. Conscious effort is impossible during sleep. Some patients with atrophy of all the striated muscles of the perineum due to injury to the spinal cord or *cauda equina* empty their bladders reflexly without any incontinence. Contraction of the striated urethral muscle can be vigorous, but this strong activity can be maintained for only a few seconds. This can be tried by anyone with the external anal sphincter. Specially prepared post-mortem specimens show that the urethra is invested with circular and longitudinal coats of smooth muscle from the bladder neck to the distal aspect of the triangular ligament. The prostate is a glandulo-muscular mass, which is inserted, as it were, into the smooth muscle distal to the bladder. Throughout the whole length of the posterior part of the urethra, smooth muscle makes up the bulk of the urethral wall anterior to the prostate, but within its capsule proximally are a few fibres of striated muscle. As the triangular ligament is approached, these fibres become greater in number and extend more and more laterally until, between the layers of the triangular ligament, they completely encircle the urethra. Wherever striated muscle lies, smooth muscle lies within it, intimately investing the urethra. Observations on patients who have suffered loss of the triangular ligament from injury show that this structure with its enclosed striated muscle is unnecessary for maintenance of continence. It is often noted that vigorous voluntary contraction of the external sphincter can interrupt the leakings of incontinence, but, since such strong activity is possible only for a few seconds, this interruption is but short. The conclusion seems inescapable that post-operative incontinence is due to excessive removal of smooth muscle in the vicinity of the prostatic apex. Surgical correction in the female is a fairly feasible procedure, but in the male a distinct lack of success has marked most of the efforts made so far. Elliot states that a logical approach would be to plicate the urethra in the vicinity of the prostatic apex, that is, just proximal to the triangular ligament, in order to increase the passive or unconscious urethral resistance in this area. He has made four such attempts; two were temporarily successful, but ultimately all were failures.

[1] *J. Urol.*, January, 1954.

Abstracts from Medical Literature.

RADIOLOGY.

Gastro-Œsophageal Incompetence in Children.

ROY ASTLEY AND IVO J. CARRE (*Radiology*, March, 1954) state that gastro-œsophageal incompetence due to a "short œsophagus" and a minor degree of partial thoracic stomach is a not uncommon cause of vomiting in infancy. The vomiting usually dates from the neonatal period, and in many cases the vomitus contains altered blood from time to time. In early infancy the vomiting is often projectile, and there may be visible gastric peristalsis, making differentiation from hypertrophic pyloric stenosis important. Weaning to solid food frequently brings improvement, and, if this occurs, symptoms usually cease by the age of about two years. If weaning brings no improvement, a longer course is likely. In a small proportion of cases of the latter group, an œsophageal stricture develops, secondary to reflux œsophagitis. Radiological diagnosis consists of the recognition of gastro-œsophageal incompetence and the identification of stomach above the diaphragm. The latter depends mainly upon the detection of the site of change of an œsophageal to a gastric mucosal pattern. Although sometimes the radiological diagnosis may be easy, it often requires considerable care and experience. Several examinations are sometimes necessary, and in a number of cases with a suggestive history the findings remain radiologically negative. Complications that may be recognized radiologically include œsophageal spasm and ulceration, stricture formation, impacted foreign bodies and pyloric abnormalities. Treatment in infancy consists of nursing in a propped-up position, maintained by a special harness. Thickened feedings are given if vomiting is persistent. Early diagnosis and treatment may reduce the incidence of complicating œsophageal strictures.

Angiography and Intracerebral Metastatic Tumours.

SVEN ETHELBERG AND KJELD VAERNET (*Radiology*, July, 1953) consider that on the evidence of the angiogram alone, a diagnosis may be arrived at both as to localization and as to pathology of intracerebral metastatic tumours in two-thirds to three-fourths of the cases. They analyse a series of angiograms in 21 cases of intracerebral metastatic tumour. They state that in the majority a small almost circular opaque patch of endoneoplastic circulation was disclosed; in other instances a circular or semi-circular bundle of delicate arteries surrounded an avascular area; in extremely few cases there was no specific configuration. The area of abnormal vascularization was nearly always found in the terminal territory of a given cerebral artery, which usually was the feeding vessel. Although metastatic tumours may affect any vascular territory of the brain, the favoured localization was the parieto-occipital regions—that is to say, the areas supplied by the largest terminal branches of the internal carotid artery. The displacement of adjacent cerebral arteries was always mild. Multiplicity was rare; and the authors comment that if it occurs, it is a definite indication of intracerebral metastatic processes. The extracerebral vascular system was never involved in the abnormal configurations. The various types of metastatic tumour could not, on the sole basis of the angiogram, be differentiated from one another. The group that responds most favourably to surgical treatment—namely, metastases from renal carcinoma (hypernephroma)—is largely distinguishable from the remainder on certain definite clinical non-neurological criteria. As for the rest, in which no favourable results can be expected, the authors believe that angiography may become a useful means to avoid futile surgical intervention.

The "Collagen" Diseases.

L. H. GARLAND AND M. A. SISSON (*Am. J. Roentgenol.*, April, 1954) state that collagen diseases constitute an interesting group of disorders—from the clinical side because of their diagnostic and therapeutic challenge, from the pathological viewpoint because of recent interest in the intercellular substances, and from the radiological viewpoint because of their widespread but unfortunately non-specific nature. The last-mentioned point is particularly true of the pulmonary manifestations of the collagen diseases. The authors feel, however, that diagnostic possibilities, slim as they are, depend on an awareness of these conditions, *plus* a knowledge that the patient has a polysystemic disease. It is desirable that radiologists, as clinicians, be able occasionally to suggest the consideration of one of these diseases, on logical grounds, and be cognizant of the further studies, clinical, laboratory or pathological, required to confirm the diagnosis. At the same time, it is believed that the term "collagen" disease is one of high abstraction, to be modified or abandoned as soon as the ætiology and fundamental nature of these conditions become established. Four types of collagen disease are discussed in this paper—*periarteritis nodosa*, disseminated *lupus erythematosus*, dermatomyositis and scleroderma. In studying a patient for possible collagen disease it is desirable that particular attention be paid to the following structures: (*a*) the skin and muscles, (*b*) the heart and pericardium, (*c*) the lungs and pleura, (*d*) the abdomen and intestinal tract, (*e*) the kidneys, and (*f*) the bones and joints. The skin and muscles may show microscopic evidence of involvement in any of the four types. Histopathological changes are reportedly fairly decisive in all types except dermatomyositis, about which not enough is yet known; they are said to be most clear-cut in periarteritis, but there is divergence of opinion as to their clarity in scleroderma. The cardiac and pleuropulmonary changes are many and nonspecific. Pericardial effusion, cardiac enlargement, pleural effusion, pulmonary nodular changes and variable degrees of pulmonary œdema or fibrosis may occur. These changes may be reversible. Abdominal distension, with paralytic obstruction, may occur in the first two conditions, as may also renal enlargement. The intestinal tract changes are most conspicuous in scleroderma, notably in the œsophagus and small intestine (variable degrees of rigidity, dilatation and narrowing occur in about 50% of cases). The articular and osseous changes occur in *periarteritis nodosa*, lupus and especially scleroderma. Radiologically, they are characteristic only in the latter condition. Calcinosis is also confined largely to this disorder.

Infrapulmonary Pleural Effusions.

ROBERT L. FRIEDMAN (*Am. J. Roentgenol.*, April, 1954) states that the diagnosis of infrapulmonary fluid simulating a high diaphragm depends upon determining the position of the collection of pleural fluid and its relationship to the diaphragm. The demonstration of small amounts of unencapsulated pleural fluid requires special methods. Whenever the suspicion of fluid is aroused by a raised diaphragm, or the clinical course of the patient indicates the presence of fluid, the following should be carried out: (i) preparation of films with the patient in the recumbent position to determine the presence of minimal pleural effusions; (ii) induction of pneumoperitoneum or distension of the stomach to outline the under surface of the diaphragm; (iii) careful thoracentesis; (iv) radiological reexamination to determine the decrease in thickness of the diaphragm and fluid shadow. The pleural space between the lung and the diaphragm is normally a potential space. When fluid gravitates to the costo-phrenic sinuses, capillary action could draw fluid between the lung and the diaphragm. The following sequence of events is suggested. When a small amount of fluid is formed, it gravitates to the posterior and lateral costophrenic sulci. The capillary attraction of the visceral and parietal diaphragmatic pleura then draws the fluid into this space. The majority of effusions thus are infrapulmonary in their beginnings. As more fluid accumulates, the minority maintain the configuration of infrapulmonary fluid, but the majority spill over, as it were, and assume the outlines of pleural effusion most commonly seen and described as typical.

Structural Changes in the Lumbar Intervertebral Disks.

R. I. HARRIS AND IAN MACNAB (*J. Bone & Joint Surg.*, May, 1954) state that one of the interesting aspects of spinal pathology which has an important bearing on the treatment of backache is that the spine acts as an integrated whole and that damage sustained by one part frequently injures other structures in the spinal column. They therefore consider that disk degeneration may be associated with an extrusion of nuclear material; it may initiate degenerative changes in the posterior joints; it may predispose to tears of the posterior spinal ligaments; or it may give rise eventually to all of these lesions, any one of which may produce backache with or without sciatica. The sciatica may be referred pain or may be produced by nerve root pressure. Nerve root pressure in such instances is commonly due to an extrusion of nuclear material, but it may also be due to pressure on the nerve root within the foramen by a "squashed" disk or by a subluxated posterior joint. The authors point out that radiographs are of great value in the diagnosis of disk degeneration, and that they are of greater value in the assessment of the secondary effects that

have taken place. With the use of bending films evidence of early degenerative changes may be obtained, tears of the supraspinous ligament can be detected, and abnormal movements of the posterior joints can be seen. Careful study of the antero-posterior and lateral projections will reveal evidence of subluxation of the posterior joints, chip fractures and degenerative arthritis in the zygapophysial articulations, and will clearly demonstrate overriding of the facets. The authors consider that the investigation of subjective phenomena, such as backache, is fraught with many difficulties, and it must be preceded by an investigation of the anatomy of the part and the anatomical variations, the normal and abnormal physiological states and the pathological lesions that occur. Many of these changes may have no clinical significance, but it is only with a knowledge of what may occur that the problem of low back pain can be tackled on a logical basis.

PHYSICAL THERAPY.

X-Ray Therapy for Cancer of the Larynx and Laryngopharynx.

W. HARRIS, S. M. SILVERSTONE AND R. KRAMER (*Am. J. Roentgenol.*, May, 1954) review twenty years' experience at the Mount Sinai Hospital, New York, in the treatment of carcinoma of the larynx and laryngopharynx. From 1931 to 1951 X-ray therapy was used as the method of choice in 220 cases. The carcinomata have been classified into two major anatomical groups, intrinsic and extrinsic, there being 117 in the first group and 103 in the second. In the intrinsic group there were 31 carcinomata originally suitable for laryngofissure and 86 which would have required laryngectomy had they been treated surgically. A histopathological report of squamous-cell carcinoma was obtained in all cases except two, in which it was adenocarcinoma. Until 1947 treatment in all cases was with 200 kilovolt irradiation through two directly opposing lateral neck fields for a mid-laryngeal tumour dose of 4700*r* to 6000*r* in twenty-eight to forty days. Since 1947 the technical change has been in the direction of higher kilovoltage, greater tumour dose and longer protraction. Five-year results are given, based on 139 cases in the period from 1931 to June, 1947. In this series there were 78 patients with limited lesions, localized to the intrinsic larynx, false cord or epiglottis with good mobility of the larynx and without laryngeal obstruction. The determinate five-year cure rate in this group of 78 is 83%, but 13 patients are untraced, and the absolute cure rate is 69%. Forty-eight of the patients would have required laryngectomy had they been treated surgically originally, and it is noteworthy that 39 of these 48 patients (over 80%) not only are alive and well, but are in full possession of their larynx with voice unimpaired. Over the whole series of cases, the determinate five-year cure rates were 59% to 77% for the intrinsic group and 41% for the extrinsic. The absolute cure rates were lower because of untraced patients. Analysis of the details about the untraced patients shows more than half of them to be over seventy years of age. Patients with laryngeal obstruction necessitating tracheotomy before or during therapy have a very poor prognosis. The ten-year results of treatment are essentially similar to those at five years and include an appreciable number of cases of advanced carcinomata. Surgical procedures are possible in case of failure after a properly administered course of radiation therapy, with successful outcome in a small number of cases. It is concluded that since the value of radiotherapy is practically the same as surgery, as far as survival is concerned, radiotherapy should be the method of choice where it is a matter of preservation of the larynx.

Convergent Beam Therapy.

O. CHANCE AND J. E. O'CONNOR (*Brit. J. Radiol.*, March, 1954) give a preliminary report on the results obtained from convergent beam therapy which they have been using for one year. For this type of therapy it was regarded as essential that the tumour should be of limited size and remain fixed during treatment, and that the method should be used to treat the tumour only and not its glandular fields. At first it was decided to use the treatment only in cases of carcinoma of the bladder in which excision, fulguration or radon seed implant was contraindicated, and in certain cases of bronchogenic carcinoma and pituitary tumours. However, as experience was gained, it was found that the method was applicable to tumours occurring in the tonsil, fauces, naso-pharynx, middle ear and maxillary antrum, and also in the isolated vertebral metastases. If possible, the treatment is planned with use of one skin field. As a rule, however, multiple fields become necessary. Great accuracy is necessary in locating and assessing the tumour. It is vital that the patient be placed for treatment in the same position as that used during tumour location. It has been the practice to give a daily average tumour dose of 160*r* to 200*r*. The total average tumour dose in the cases described was 5000*r* to 7000*r* in thirty-five to fifty days. Eleven patients with advanced carcinoma of the bladder were treated. In every case the urologist believed that the alternative to radiotherapy was total cystectomy. All eleven patients completed treatment. In six of them cystoscopy from six to ten months after therapy revealed no evidence of active growth. Some details are given of patients with tumours in other sites who showed improvement after therapy. The most striking finding is that the general well-being of the patient appears to improve throughout the course of treatment. This is presumably due to the low integral dose. Convergent beam therapy is regarded as a relatively simple and economical method of treating certain deeply seated growths.

Intracranial Tumours in Children.

J. JACKSON RICHMOND (*J. Fac. Radiologists*, January, 1953) states that increasing knowledge has accumulated concerning the behaviour of the gliomata to ionizing radiations. Earlier treatment by radiotherapy was often too conservative. Radiotherapy is a weapon of the first importance, particularly when it is considered that radical extirpation of a malignant glioma is feasible in only a small proportion of cases. The author reviews a series of 110 cases of intracranial tumours in children which came under his personal care during the previous ten-year period. The sex and age incidences are discussed and compared with those in an adult group of 560 patients treated during the same period. The presenting symptoms, anatomical sites of origin and pathological classification of the tumours are given, and principles of irradiation techniques and general management are outlined. For patients twelve years of age and over, a minimum tumour dose of 4000*r* in four weeks is given if possible. For a baby of one year, 50% (2000*r*) is the dose prescribed, and for a child of five years 3000*r*. Of the 110 children, 45 have died and two remain untraced. Of 67 patients treated three or more years ago, 34 are alive. Of 53 patients treated four or more years ago, 26 are alive, and of 32 patients treated five or more years ago, 17 are alive. The author states that in view of the serious nature of most intracranial tumours, these results are at least extremely heartening and indicate that the therapy has been well worth while. Although the numbers comprising individual types of gliomata are too small to allow rigid conclusions to be drawn, it should be noted that the five-year survival rate in the medulloblastoma group is 43%, and in the highly malignant glioblastoma group 33%. Clinical records of six patients are given.

Hepatic Metastases.

R. PHILLIPS, D. A. KARNOFSKY, L. D. HAMILTON AND J. J. NICKSON (*Am. J. Roentgenol.*, May, 1954) state that metastatic cancer is found in the liver in about one-third of the subjects of malignant disease coming to autopsy, and hepatic failure is often the cause of death. Liver metastases have been regarded as a hopeless proposition for radiotherapy, mainly from fear of irreversibly damaging the surviving liver parenchyma. The authors report the results of treatment of hepatic metastases secondary to carcinoma of the breast, bronchus and gastro-intestinal tract in 36 cases. With one possible exception none of the patients had radiation damage to the liver parenchyma. Extensive liver function studies have been carried out in most of the cases. Symptomatic improvement was obtained in 26 cases, and was shown by relief of pain, anorexia, nausea, vomiting, weakness, fatigue, sweating and abdominal distension, and was accompanied by reduction in the size of the enlarged liver, by gain in body weight, and by improvement in liver function as measured by determination of serum bilirubin, alkaline phosphatase, cholesterols and proteins, and by the bromsulphthalein retention test, determination of the prothrombin time and other tests. The method of treatment was supervoltage X-ray therapy, at one million volts, alone in 22 cases, and supervoltage therapy preceded by a single intravenous dose of nitrogen mustard (0·4 milligramme per kilogram of body weight) in 14 cases. The whole liver was irradiated through opposed anterior and posterior fields, and the tumour dose ranged from 2000*r* to 3750*r*. The over-all time of treatment was eight days in 24 cases, fifteen days in six cases, and twenty-two days in six cases. The dose levels of 3000*r* and 3750*r* carry a risk of damage to the gastro-intestinal mucous membrane, particularly that of the transverse colon. The longest period of survival was seven months.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

CVIII.

BREAST FEEDING.

Suck, baby, suck! mother's love grows by giving:
Drain the sweet founts that only thrive by wasting.
—CHARLES LAMB.

IF it is true, as Richardson say, that "the most formidable of all obstacles to breast feeding is the indifference and at times the actual opposition of a large segment of the medical profession", then I cannot hope that many will read this article. However, the question of whether a mother is to breast feed her baby or not must be answered to the satisfaction of everyone, herself, her doctor and, though often overlooked, her baby. I have sufficient faith in my profession to think that basically every general practitioner and obstetrician has at heart the health and happiness of the mother and child in his care. I can only assume that it is ignorance or lack of thought that leads so many doctors to supervise pregnancy and the pre-natal health of the baby with such care and take no apparent interest between delivery, or perhaps the discharge of mother and baby from hospital, and the sixth week, a period fraught with much danger to the baby and much discomfort to the mother, when most of her lactational problems, including breast infections, occur. I hope that in discussing this subject I shall be able to dispel some of the ignorance and also avoid the almost religious fervour to which even I, at times, appear to succumb when infant feeding is mentioned.

Scientific artificial feeding is now an established fact. Scientific breast feeding is only in its infancy, but we have sufficient scientific information about breast feeding at our disposal for any doctor to make himself familiar with a satisfactory technique and to be able to decide unemotionally when it is advisable for a baby to be breast fed and when other methods are preferable, without having to refer to his own wife or be dominated by her ultimate solution to her lactation problems. All that he requires is some understanding of the anatomy and physiology of lactation, which I shall try to put in a useful form, and a lot of patience and understanding of human nature. He will then be able to assist the majority of women to enjoy breast feeding their babies.

Reasons for Breast Feeding.

I feel that most of the arguments that have been waged on the pros and cons of artificial and breast feeding are of little consequence. Much of the statistical evidence is fallacious because of the failure to consider multiple factors; so that, though one side claims fewer criminals and finer athletes for breast feeding and the other bigger and more calcified babies for artificial feeding, I think it wiser to take the rational approach. Breast milk is the food that Nature provided for babies; it cannot be made in the laboratory or completely replaced despite our ever-increasing knowledge of its constituents. It is surely then only common sense to make all reasonable efforts to give the baby the food Nature intended, consistent with the needs of the mother in our complex civilization.

There is adequate evidence available that the importance of breast milk varies in accordance with the age of the baby, and, at least for the first three months of life, breast feeding is an important factor in prevention of severe and fatal illness. Breast feeding is also a source of pure physical pleasure, basically sexual. The happiness and exhilaration associated with relaxation and relief of tension that accompany a normal breast feed is the right of every mother, and of great importance to the woman in the puerperium. There is increasing evidence that establishment of successful breast feeding is a step in the right direction in maintaining the mental health of both mother and child, and with the increasing realization of the importance of the stable family group it is receiving support from unexpected sources, from anthropologists to educationalists.

I doubt if one can any longer argue that breast feeding is easier than artificial feeding in the first two months, because establishment is not always a simple uncomplicated process in modern women; however, it is undoubtedly true that established lactation is easier than artificial feeding.

In periods of financial depression there is usually an increase in the incidence of breast feeding, though bad social conditions cause a decrease. It may therefore be deduced that where the pennies have to be counted without undue anxiety, breast feeding does work out more cheaply than bottle feeding; in any case it has the enormous advantage that one good high-protein diet with adequate vitamins and minerals means a healthy mother as well as a healthy child.

Those who have to return to work for financial reasons should be persuaded to wait till the baby is established on artificial food; even one month with the child on the breast makes this much easier and is worth while. Women who for social or sartorial reasons have decided not to breast feed their babies will often change their minds when they see the baby and discuss the pros and cons, particularly if three months is the aim. The woman with the possessive mother and the woman whose doctor's wife failed to breast feed her babies are both in danger of not getting a chance to fulfil their normal functions. Previous breast abscesses and cracked nipples are not contraindications, though the woman may have decided that they are, as both are usually preventible by adequate preparation in the ante-natal period.

Anatomy and Physiology of Lactation.

Four stages of lactation may be considered: (*a*) pre-natal phase, (*b*) initiation, (*c*) establishment, (*d*) maintenance.

During pregnancy the breast develops under the influence of stilbœstrol, progesterone and anterior pituitary secretion, so that by six months there is a complex secretory system consisting of alveoli, ducts, sinuses and nipple ducts surrounded by contractile myoepithelial cells and supported by fat and connective tissue. The placenta stimulates both secretion and growth. As the adrenal also appears to do so it is not possible to differentiate the individual roles of each gland. It does appear that the placenta exercises an inhibitory effect and that its removal is necessary for initiation of milk secretion. The combined effects of adrenal cortical activity, prolactin and ACTH then initiate secretion. Hormonal substitution therapy has so far proved disappointing, but retained placental fragments inhibit lactation, presumably by inhibition of secretion. Initiation may be delayed by obstetrical complications, such as Cæsarean section, difficult instrumental delivery, post-partum hæmorrhage, toxæmia and stilbœstrol medical induction of labour.

With the initiation of milk secretion, the expulsive milk ejection reflex (draught or "let down") also becomes effective. This reflex appears to consist of a sensory path from nipple to hypothalamus and posterior pituitary lobe, resulting in the secretion of posterior pituitary hormone, which acts as a chemical stimulant to the contractile myoepithelial cells surrounding the gland tissue. In the establishment period it may be initiated by psychological stimulation, such as thinking of the baby, as well as sensory stimulation of the nipple by suckling or handling, and by full breasts. Pain and emotional factors, such as fear, anger and embarrassment, probably acting through the sympathetic, will inhibit the reflex. *Multiparæ* recognize it as a subjective sensation of "pins and needles" in the breast occurring just before or at the beginning of feeds from the onset of lactation, but *primiparæ* may not feel it for several weeks.

The establishment period lasts about four weeks in *multiparæ* and up to eight weeks in *primiparæ*; and it is during this period that the milk production is stabilized, supply equalling demand, and the draught reflex becomes conditioned, so that stimulation of the nipples, preferably by suckling, causes regular "let down" of the milk. Both secretion and expulsion of milk are dependent on adequate stimulation of the nipples at sufficiently frequent intervals. Inadequate emptying will cause a fall in secretion.

Maintenance of lactation depends on complete emptying of the breasts, adequate stimulation of the draught and secretory reflexes, and relief of inhibitory factors. Five or six feeds a day are necessary during the establishment period, and comparatively few women can continue if a twelve-hour night interval is observed before the end of three months. There are a few patients with endocrine imbalance who fail to initiate lactation and some whose lactation is consistently inadequate. There is evidence that those who are underweight and on inadequate diets will also fail. Women doing heavy work and those subjected to undue psychological stress also find maintenance difficult.

Milk Composition.

There is considerable variation in milk composition between individuals, and this, together with the difficulties in collecting a full twenty-four-hour milk sample with normal draught reflexes occurring, makes milk analysis a useless procedure for anything but research purposes where collection of samples can be adequately supervised.

Average figures for the main constituents of milk are as follows: Fat: 3% to 4% (with a diurnal variation). Protein: 1·0% to 1·5% (ratio of lactalbumin and lactglobulin to casein in 2:1, which renders it much more digestible than cow's milk). Sugar: 6% to 7%. Vitamin content: adequate provided the mother's diet is adequate in vitamin *C* and riboflavin content. Minerals: calcium, 14 to 49 milligrammes per 100 millilitres; phosphorus, 10 to 20 milligrammes per 100 millilitres; sodium, 11 to 19 milligrammes per 100 millilitres; potassium, 48 to 65 milligrammes per 100 millilitres; iron, 0·09 to 0·2 milligramme per 100 millilitres.

Pre-Natal Preparation for Lactation.

The following pre-natal preparation for lactation should be made:

1. Examine the breasts at the patient's first visit. Note any nipple abnormalities, such as inverted retracted nipples, or nipples that cannot be easily pulled forward (poor protraction). Discuss the question of the desirability of breast feeding.

2. About the twentieth week start preparation. Wash the nipples daily with warm water, then cold, and rub with a towel. Draw out the nipples between finger and thumb, using lanoline. Use nipple shells or aerators for inverted nipples. No scrubbing should be used and no treatment should be painful.

3. Teach breast massage and pre-natal expression of colostrum for five minutes daily from the thirty-sixth week or earlier if difficulty is expected. Advise a suitable uplift brassière with wide adjustable shoulder straps and front opening.

Management of Lactation.

In the Maternity Hospital.

It has been demonstrated that preparation for breast feeding doubles the incidence of breast feeding, but only if combined with good supervision of the hospital period. Mothers must be shown good breast feeding technique—that is, the baby held close, with head supported and good airway, the mother relaxed and supporting the breast with the nipple and part of the areola in the baby's mouth. The first feeds must be short practice feeds, timed by the clock, one to three minutes in length, as sucking at an empty breast is a certain way to cause cracked nipples. It is more important to wash the hands before feeding than to wash the nipples.

The hospital sister should inspect the breasts and nipples frequently to detect nipple abrasions and make sure that one breast at least is emptied each feed; manual or pump expression after feeds should be practised if the baby is not doing this. The best way to determine the baby's intake is by test weighing, but it is better for the mother not to know the results. There is probably no greater depressant to lactation than a militant nurse who grimly informs the emotional mother that "baby didn't get enough that feed", and tells her to "put it on again". The woman in the puerperal state is emotionally unstable, and thoughtless remarks and complicated instructions will greatly disturb her lactation; she needs constant encouragement and kindness.

There seems no doubt from experiments too numerous to mention that it is in the interests of both the average baby and his mother's breasts for him to have six feeds daily once the milk has come in. Feeds prior to that are short feeds at less frequent intervals. Some women with large sinus systems and elastic skins are able to establish lactation even on four feeds a day, but they are a decided minority, and even some of these fail from lack of stimulation within three months. In the neonatal period the baby recovering from a stormy passage into this world will often fail to empty the breast, and unless routine hand expression or routine test weighing is done, lactation may fail. Complementary feeding should be kept to a minimum and calculated on the twenty-four-hour milk yield and the baby's wishes.

Cracked Nipples.—Cracked nipples are of several types. Those with superficial epithelial blebs that are often petechial are commonest; those with ulcers or deep cracks at the base of the nipple are hardest to heal and most often associated with bad feeding technique and faulty nipples, but they can usually be treated. When there is extensive dermatitis including the areola, weaning is usually necessary. When there is no apparent abrasion but persistent hypersensitivity, there is usually an underlying psychological reason. If simple reassurance and discussion do not cure it, weaning is preferable to psychotherapy. Sunlight and rest are the best treatment for cracked nipples; the baby is fed with expressed milk while the nipples are rested for twenty-four hours, if necessary, short feeds then being allowed followed by hand expression. Local applications are disappointing, but *Unguentum Hamamelidis, Unguentum Morrhuæ* or *Tinctura Benzoini Composita* with *Oleum Ricini* (one part in eight) is moderately satisfactory.

Engorgement.—Engorgement may occur on the third or fourth day. It is best treated by administration of stilbœstrol, five to ten milligrammes, repeated in four hours if necessary, hand expression, which is often very difficult, warm packs and short feeds or rest from suckling for several feeds, as the œdematous nipple cracks easily. Relief of the pressure is essential, or the rising tension will suppress lactation or so damage alveolar tissue that by the sixth week the supply is failing. Pre-natal expression reduces the incidence of engorgement.

Mastitis.—The most serious complication of the puerperal period is mastitis, which should be an almost preventible condition. The predisposing factors are cracked nipples, overloaded breasts, staphylococcal infection in the baby (pustules, sticky eye, infected cord) and primiparity. It tends to be a recurrent condition, unless these factors are corrected and the primiparous patient is instructed adequately in feeding technique. The organism is hæmolytic *Staphylococcus aureus* from the maternity hospital and in most cases is now penicillin-resistant, so a tetracycline ("Aureomycin" or "Terramycin") is usually needed. Sulphonamides are contraindicated, and if the condition has been present for more than four days it is often necessary to incise it. Administration of five milligrammes of stilbœstrol and restriction of fluids are necessary if lactation is copious. It is bad treatment to wean the baby, as this tends to make the condition worse by increasing milk retention. Feeding should continue on the opposite breast and be resumed on the infected breast after expression of two or three feeds. The baby usually has an infection or is a nasal carrier and often requires treatment too.

Management After Discharge from Hospital.

Though I am content to follow a three-hourly feeding schedule in hospital with babies in nurseries to allow the *multiparæ* better rest, I think that *primiparæ* would be better "rooming in" with their babies, and I am sure that when mothers return home on their tenth day or earlier they are then well advised to relax their routine considerably. In these civilized times most city mothers, at least, live their lives by the clock. For the modern undomesticated woman it is quite a feat to plan an ordered existence, preparing meals, shopping and doing housework. As I have already indicated, the mother must have peace of mind to feed her baby satisfactorily, and such peace is rarely possible in the chaos of free demand feeding. How can her draught reflex function normally with a baked dinner getting cold on the table and a hungry husband not a little exasperated, regardless of baby's demands? On the other hand, no one with any human sympathy denies that a hungry baby must be fed; he must not be allowed to cry until he is too tired and full of wind to enjoy a meal, nor is it reasonable to wake him from deep sleep and insist on his taking food that he does not want. I have also yet to find the mother who knows for sure what her baby is demanding (grandmothers, of course, usually know, but this rarely helps the situation). I think therefore that a happy compromise is possible and advise six or seven feeds in twenty-four hours—that is, approximately three-hourly—until the baby has regained his birth weight, and then approximately four-hourly—that is, five or six feeds in twenty-four hours. For the first six weeks an additional night feed may be necessary, though most babies are content with a 6 p.m. feed and one during the night, usually about midnight. A longer night interval is unphysiological, and the practice of giving boiled water has little to recommend it. It is advisable to adopt a routine as soon as practicable and this is best done gradually, and takes about six weeks. The same relaxed approach applies to duration of feeding. It is quite unreasonable to say that a baby should feed for ten minutes on each side, though this is an average figure. It is also unscientific to expect or allow a baby to continue to suck after the milk as gone; in the early stages this merely means sore nipples and wind. However, woman's notoriously vague ideas about time are considerably vaguer when she is lactating, and I still find a watch an essential part of her feeding equipment. Many babies will get a good feed in ten minutes; no normal baby should take an hour.

The baby should be fed in a peaceful atmosphere, the mother relaxed, comfortable and unhurried. There is no doubt that the mother can transfer her anxiety to the baby,

and many mothers are better with a mild sedative, such as phenobarbital, half a grain twice a day for a few weeks.

It is also essential that the mother should master the technique of "getting up the wind" and that she should understand that all the wind the baby gets is swallowed and mainly preventible by good feeding technique. It takes three months for a woman to return to normal mentally and physically, longer after a first baby, and she is too often expected to resume her normal duties in ten days with serious results for her lactation. The lactating woman must have rest. She must also have adequate fluid and a high-protein diet. It is not necessary to give copious fluids; it is sufficient only to satisfy thirst, including one and a half or two pints of milk daily, taken as milk coffee or better still with some vitamin preparation, such as "Akta-Vite", before the baby's feed. The common practice of drinking large quantities of water appears to have no scientific foundation. A recent investigation carried out at a mothercraft home indicated that mothers enjoyed "Akta-Vite" in milk and were readily taking both milk and vitamins. There is no evidence that any of the much advertised proprietary preparations for stimulating milk production are effective in any other way than psychologically. In anæmic women iron acts as a galactogogue. The present vogue amongst obstetricians of limiting weight gain during pregnancy to less than 27 pounds, regardless of size and shape of patient, means that many women now start their lactation very little above or even below their non-pregnant weight, and many of these fail early. I am afraid that Avicenna, whose rules for selection of a wet nurse still hold good today, would have rejected many of these poor bony creatures in favour of more buxom wenches. At least I appeal to obstetricians to give written detailed diets and not to risk the periods of semistarvation practised by some women to keep within the permitted weight gain. Women should not lose subcutaneous fat during pregnancy.

Weaning.—The baby should be introduced to mixed feeding at about the twentieth week, when the sucking reflex is becoming less active; and by the time weaning is to be commenced, between the seventh and eighth months, at least half the caloric intake should be from other foods than breast milk. Weaning should be a gradual process. The night feed should have been stopped before the fifth month or earlier if the baby was sleeping through the twelve hours and the mother's breasts were not too full. It is usually possible to replace one feed per week with a substitute any time after the seventh month, and stilbœstrol should not be needed to help suppress lactation.

Underfeeding.—Underfeeding is characterized by crying, small stools, failure to gain in weight and often an appearance of alertness and anxiety in the child. It is best corrected by complementary feeding; and if less than half the total feeding for the day is required, it is worth while for two months. Frequently it is necessary to complement only the 6 p.m. and night feeds, and it is usually preferable to let the baby determine the quantity rather than let the mother use scales. Also single test weighings are often fallacious and have been the cause of weaning many babies unnecessarily. The mother goes to the health centre for a "test weigh" much as she would to an examination, and anxiety and unfamiliar surroundings often inhibit the draught. If the sister does not appreciate this and the fact that there are considerable normal variations in quanity from feed to feed, wrong advice will be given. I think that most mothers find the proprietary dried milk preparations easier to use than diluted cow's milk for complementary feeding, but the latter is satisfactory. Additional vitamins are also necessary, being most easily given as "Pentavite", five to ten drops daily.

Overfeeding.—Overfeeding is a dubious entity and rather a bogy except in the first month, when a baby can be forced to overfeed with resultant restlessness and frequent stools. More often vomiting, colic and frequent stools are due to rapid feeding and a forceful or irregular draught reflex, and can be corrected by mild sedation of the mother and by "bringing in the milk" by manual stimulation of the nipple before starting the baby's feed. It is also helpful to use some method of posture feeding that puts the baby in a better position to cope with the rapid flow of milk, for example, mother lying down or the baby being tucked under the arm "twin fashion". Shortening the duration of feeds and using one breast only at a feed are both unsatisfactory measures that may result in failure of lactation unless used intelligently, as they can cause overloading; some milk must always be expressed from the unused breast. Big weight gains, such as one pound per week, should never be regarded as evidence of overfeeding in an asymptomatic baby in the first three months.

Contraindications to Breast Feeding.

There are some women who do not enjoy breast feeding, just as there are some who do not enjoy other normal sexual activities. The majority of these will, however, feed their babies for a short time, but a few have a deep-seated psychiatric antipathy, which may manifest itself as intensely tender nipples without local lesion or as outright refusal to feed the baby. These women should never be urged to persist with breast feeding and should be helped to feed their baby artificially without a sense of guilt.

Tuberculosis is an absolute contraindication to breast feeding, which is undesirable within five years of healing of a tuberculous lesion. In fact it is probably preferable that no woman who has had tuberculosis should breast feed her first baby; fatigue, emotion and decalcification are friends of the tubercle bacillus.

Chronic nephritis and chronic cardiac disease usually indicate that a short lactation is desirable. Acute illness in the mother and puerperal psychoses usually necessitate weaning. Diabetes is not a contraindication, though diabetics usually fail to lactate satisfactorily.

Conclusion.

I should like to stress that the consistent sympathetic supervision that is necessary for lactating women is time-consuming and often irritating, and the general practitioner is well advised not to undertake it himself. If he is willing to supervise pre-natal preparation and lactation in the maternity hospital (or to let a pædiatrician do it), he can provide continuity for his patient by close cooperation with the health centre sisters. It is the policy of the Health Department for Baby Health Centre sisters to supervise normal management of babies and to carry out whatever method of feeding the patient's doctor orders. If doctors would discuss their reasons for feeding and weaning and communicate them by letter or telephone rather than by the dubious medium of the mother, I am sure a much happier relationship would exist between doctor and sister. This also assumes that in return those responsible for the training of these sisters must see that they are familiar with proprietary infant foods and their uses in addition to the commoner methods. The complaint that "all most doctors know about breast feeding is how to wean" may often be regrettably true, but it is equally true that some health centre sisters will not supervise feeding with "Nestogen" or "Glaxo 1" or permit a night feed after 10 p.m.

I trust that this article will encourage a more relaxed attitude to the management of breast feeding and will inspire more doctors to cooperate amicably with the health centre sisters in an effort to establish and maintain lactation for those 80% of women who are physically and psychologically capable of feeding their infants.

CLAIR ISBISTER,
Sydney.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal North Shore Hospital of Sydney, Crow's Nest, New South Wales, on April 22, 1954. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital. Parts of this report appeared in the issues of July 31 and September 11, 1954.

Supraspinatus Calcification.

DR. T. F. ROSE presented four patients to illustrate some aspects of supraspinatus tendon calcification. He said that what caused supraspinatus tendon calcification was not fully known. It was thought to occur in supraspinatus tendinitis, often in old people, as a degenerative process, but it might occur in adults of all ages, sometimes after a history of only mild injury. It might also be accompanied by calcification in the tendons of the infraspinatus and the *teres minor* muscles, as in the third case. It was probable that the calcification was present before the incident or incidents causing symptoms occurred, because calcified deposits could exist deep in the tendon without symptoms. When those deposits (amorphous calcium carbonate and phosphate) were forced out of the tendon by, say, a sudden contraction into the tissue beneath the subacromial wall, which was well

supplied with sensory nerves, then pain occurred. That was illustrated in the second case, in which the patient had calcification in both supraspinatus tendons but symptoms at first in only one. Later, when extra work involved the symptomless shoulder, it became painful. In none of the other three cases was the opposite shoulder affected. The fourth case differed from the others in that while the calcified deposits in those were of toothpaste consistency with a normal subacromial bursa, the deposit in the fourth case was a hard cartilaginous-like mass and there were degenerative changes in the subacromial bursa and the shoulder joint as well.

The first patient, a man, aged sixty-six years, had performed some unaccustomed work in shifting trestle tables. This was immediately followed by mild aching pain over the left deltoid region for four days. Then the pain became suddenly severe, running down the outer aspect of the limb to the hand. This pain was worse on abduction movements, so that he was unable to abduct his shoulder voluntarily. Examination of the patient showed that he was very tender over the left deltoid beneath the acromion process. X-ray examination showed a small calcified plaque situated in the region of the insertion of the supraspinatus tendon. In the other shoulder was symptomless calcification in the subacromial bursa. Conservative treatment was employed. The arm was placed in a sling, and no abduction movements were allowed until the pain went. This it did in ten days, and the shoulder had since been normal for three months. Six weeks after commencement of the illness, X-ray examination of the left shoulder showed the supraspinatus calcification to have completely disappeared, which showed that the deposits could undergo absorption of their own accord.

The second patient, a married woman, aged thirty-eight years, was a right-handed "A" grade tennis player. Twelve hours after a particularly hard match she developed severe pain on the outer aspect of the right shoulder. This lasted continuously for five days and was so severe that she could not sleep, nor could she move the shoulder. The pain then lessened at rest, but abduction movements always caused an acute exacerbation of the pain. Examination of the patient showed the usual tender area with inability to abduct the shoulder. X-ray examination of both shoulders revealed calcification in both supraspinatus tendons. At operation, a mass of gritty, toothpaste-like substance was curetted from the right supraspinatus tendon. This substance was examined microscopically, and the pathologist stated that it was calcification in fibrous tissue. The pain was relieved immediately, and full movements, including abduction, were present in six weeks. Since the operation, the patient had used her left arm more than usually, so that eventually she had the same pain in the left shoulder, though not of such intensity. A similar operation was performed twelve months later, with immediate relief of pain and early return of shoulder movements as on the other side. In order to avoid further similar strain on the shoulders, the patient then gave up tennis. There had been no recurrence of symptoms for the past three years in the right and the past two in the left shoulder. Unfortunately no post-operative X-ray films were taken, and the patient had now left the State.

The third patient, a married woman, aged thirty-eight years, whilst doing domestic duties, had experienced an aching pain on the outer aspect of the right shoulder for some two years prior to seeking advice from Dr. Rose. The condition had been said to be a supraspinatus calcification (X-ray films were unobtainable) and had been treated with saline injections with symptomatic relief of pain. Two years later, whilst she was working a factory lathe, this became stuck, and to make it move she hit it repeatedly with her right hand. The next day she developed severe pain over the outer aspect of the right shoulder with tenderness and loss of abduction. X-ray examination showed extensive calcification in the tendinous attachments to the greater tuberosity of the humerus, both superiorly in the supraspinatus tendon and posteriorly in the infraspinatus and the *teres minor* tendons (in other words, a very widespread calcification which had obviously been present for some time). At operation as much calcified "toothpaste" was curetted out as possible. Pain was relieved immediately, and full movements were present in three months. Then, one day, three months after operation, the patient hung out the washing and some pain recurred, though for two days only. An X-ray examination then showed that much calcification had occurred. However, the shoulder had now been symptom-free for the past six months. The incident was a salutary warning to the patient against extreme abduction.

The last patient of the group was a hard-working woman, aged sixty-three years, who had had pain in the lateral aspect of the right shoulder for eight months. The pain was becoming worse and was intensified on abduction of the arm. Examination of the shoulder disclosed tenderness over the deltoid below the acromion process with loss of abduction because of the pain it caused. X-ray examination showed a calcified mass in the region of the tendon of the supraspinatus. The joint surfaces were normal. The left shoulder joint was normal. At operation, the mass was removed from the supraspinatus tendon. As it was a hard plaque, it had to be cut from the tendon, with consequent exposure of a small portion of the articular surface of the humerus. It was noticed that the cartilage there was pitted. The subacromial bursa, which was so large that it had to be traversed to reach the tendon, was the seat of chronic inflammation, in that its walls were thick and reddened with papillary-like folds projecting into its interior. Pain disappeared immediately after operation, and movements six weeks later were returning well, with abduction last as usual. X-ray examination now showed no visible calcified mass. Dr. Rose said that the possibility of recurrence must be considered in this case, as in all the others, if the patient had to carry on with her work which involved heavy washing. In any case, calcification might occur even if it caused no symptoms.

In a general discussion Dr. Rose said that symptoms in all the cases were the same, namely, pain, worse on abduction, on the outer aspect of the shoulder which in the first case radiated down the outer aspect of the upper limb to the hand. There was tenderness below the acromion with diminution or absence of abduction because of the pain it elicited. The cases showed well that whilst sometimes conservative non-operative treatment only was required, usually more active measures were necessary; for instance, injection with saline successfully relieved symptoms in the third case. Operation (exposure and removal of the mass either in its amorphous toothpaste-like form or in its harder form) relieved pain immediately. Movements, especially abduction, took longer to return (up to three months or more) because of the surgical trauma to the deltoid and supraspinatus muscles. With regard to prognosis, it was necessary to realize that the deposits could be renewed, and, if further strain was applied to the supraspinatus tendon, cause further pain.

Gastro-ileostomy.

Dr. Rose then referred to the case of a married woman, aged sixty-six years, who had had a partial gastrectomy performed elsewhere for "ulcers" three months prior to admission to the Royal North Shore Hospital of Sydney. Within a week of operation she had commenced to suffer attacks of diarrhœa with pale, bulky, offensive stools, and some abdominal distension. The illness became worse, and she became emaciated because she could not take food (even milk); as soon as she did so, within an hour or so she would have a large loose stool, at times with food debris mixed in it. At the time of admission to hospital, she was very ill and starved and was incontinent of fæces. Her breath was not as foul as that of a patient suffering from a gastro-jejuno-colic fistula, nor had she ever vomited fæces. She had not suffered from tetany, nor had she been œdematous. On examination she was seen to be a very emaciated woman with a very small recent upper right paramedian incision. There was no œdema anywhere, and the abdomen was not distended. X-ray examination with barium meal and enema revealed that gastro-ileostomy had been performed after partial gastrectomy. Blood examination revealed microcytic anæmia, the red blood cells numbering 3,500,000 per cubic millimetre. The serum protein concentration was normal, as was the albumin-globulin ratio. The blood electrolyte concentration was strangely normal by photometric analysis, the serum sodium and chloride concentrations being normal. The serum potassium concentration was, however, low, and this was confirmed by electrocardiography. Observation showed that as soon as any food was eaten the patient had an attack of uncontrollable diarrhœa. The fæces were fluid and yellow in colour, and at times undigested food of the previous meal was passed. When fluids only were given, the diarrhœa stopped. After blood transfusions and parenteral therapy, including the administration of potassium, operation was performed. There was found an end-to-end anastomosis between the stump of the stomach and the terminal part of the ileum, not six inches from the caecum. There was no evidence of ileal ulcer. The anastomosis was undone, the ileum sutured, and a correct antecolic anastomosis formed between stomach remnant and jejunum. Unfortunately, the patient went into apnœa on the following day and died.

Dr. Rose commented that it was difficult to conceive how the mistake could have occurred as the duodeno-jejunal flexure was usually easy to find. Nevertheless, reports of such an error were constantly being found in the surgical

literature. In the present instance the very small incision in the skin might have caused the error.

Submucous Lipoma of the Hepatic Flexure with Recurrent Intussusception.

Dr. Rose then showed a married woman, aged forty-five years, who had had recurrent attacks of right-sided colicky abdominal pain at irregular intervals associated with frequency of micturition for two years. Repeated general examinations, an excretion and a retrograde pyelogram, and two X-ray examinations after barium enema had revealed nothing abnormal. Then the patient noticed that every time the pain recurred, she could feel a tender mass on the right side of the abdomen. It disappeared with the cessation of the pain. When she was examined in an attack of pain, a tender, vague, rather diffuse mass could be felt in the right lumbar region. When the pain ceased, this could not be palpated. A further X-ray examination after barium enema revealed a large filling defect in the hepatic flexure. Operation revealed a large submucous lipoma in the ascending colon and hepatic flexure, which was causing an intussusception. This had never progressed far because the ascending colon did not have a mesentery. Owing to the size of the lipoma a right hemicolectomy had to be performed for its removal. The patient had been well for the two years following operation.

Acute Small Bowel Obstruction due to Unripe Blackberries.

Dr. Rose then showed a woman, aged fifty years, who some hours after over-indulgence in partially ripe (red) blackberries had suffered severe abdominal colic with vomiting (but not of blackberries). This was followed by abdominal distension. She was first examined twelve hours after her meal. The abdomen was diffusely distended in the form of a small-bowel ladder pattern, with visible peristalsis most marked on the left side of the abdomen. A plain X-ray examination of the abdomen showed fluid levels, especially on the left side. After the passage of a Ryle's tube, and the commencement of the appropriate parenteral therapy, the abdomen was explored. In the lower part of the jejunum, a large mass of gritty foodstuff was found, the bowel above it being distended and that below collapsed. This mass was able to be broken and squeezed further down the intestine with the fingers without the bowel having to be opened. Convalescence was uneventful, and a three-month follow-up revealed no further symptoms.

Undiagnosed Lesion of Lower Femoral Epiphysis.

Dr. Rose's next patient, a boy of eight years at his first appearance at the hospital, had been treated from January, 1949, to September, 1950. He had complained that since December, 1948, he had had pain, swelling and stiffness of the left knee so that he limped. On examination he was found to be a pale, sick boy with a temperature of 101° F., a pulse rate of 110 per minute, and a furred tongue. His left knee was held rigidly in almost complete flexion. The knee was swollen and tender and was full of fluid. It was white, rather than red in appearance. It was a little hot to the touch. X-ray examination showed a rounded area of translucency in the medial femoral condyle. Mantoux and Kline test results were negative. The X-ray appearance of the chest was normal. A full blood count showed mild microcytic anæmia and a normal white cell count. With the patient under general anæsthesia, fluid was aspirated from the joint. This was clear fluid, which was later shown to be sterile on culture. Nothing significant was found on examination of the fluid. The knee was straightened and put in plaster for three months. The patient then steadily improved, so that his temperature was normal in one week. The leg was out of plaster in three months, and he had full walking movements of the knee in six months. Serial X-ray examinations showed a steady ossification of the lesion with no interference with growth.

Dr. Rose said that presumably the lesion must have been due to non-specific inflammation because of its speed of onset and the steady improvement. At first it looked like an acute tuberculous condition, but the X-ray appearances and the progress of the patient discounted this. The lesion was not an osteoid osteoma, because the X-ray appearances were not characteristic of that disease.

Neurilemmoma of Lateral Popliteal Nerve.

Another patient shown by Dr. Rose was a married woman, aged thirty-seven years, who had complained of a painless swelling on the back of the left thigh present for six months. This was associated with tingling on the dorsum of the foot whenever the swelling was touched. Examination of the patient disclosed a firm, rounded swelling with slight side-to-side mobility on the posterior aspect of the left thigh just above the popliteal fossa. It was deep to the hamstrings. Touching it elicited tingling in the distribution of the musculo-cutaneous division of the lateral popliteal nerve. Operation revealed a high division of the sciatic nerve into its two main divisions. A partly solid, partly cystic mass was found, encapsulated except at its upper and lower poles, where its substance was continued up and down within the nerve sheath. The mass itself had so stretched the nerve that its fibres were unrecognizable. Nevertheless, there were no objective neurological signs referable to dysfunction of the nerve. The mass and nerve trunk containing the extensions were excised, with consequent lateral popliteal palsy and characteristic footdrop. Excision was performed because the tumour substance looked malignant, being more heterogeneous in appearance than one expected in a simple tumour; also its substance was extending up and down the nerve sheath. In spite of the macroscopical appearance, the histological appearance was that of a benign schwannoma. However, watch must be gept for a further tumour. The patient also had a small, round, hard tumour in the substance of the adductor muscles on the same side. Dr. Rose said that this multiplicity was more characteristic of von Recklinghausen's neurofibromatosis than of neurilemmoma. There were no other stigmata of the former disease.

Carcinoma of the Sigmoid Colon Arising from a Polypus in an Area of Diverticulosis.

Dr. Rose showed a female patient, aged fifty years, who had had frank bleeding from the bowel for four years. Repeated X-ray examinations after barium enema showed diverticulosis, and for some reason the bleeding was attributed to this. However, the last X-ray examination showed a filling defect in the sigmoid colon, and examination under anæsthesia demonstrated a mass high up in the pelvis. At operation, the following were found in a small area of the sigmoid colon: (i) a small operable ring carcinoma with no secondary deposits, (ii) several polypi adjacent to it, (iii) diverticulosis of the segment. Resection of the sigmoid colon was successfully performed with primary anastomosis.

Dr. Rose said that obviously the diverticulosis was a red herring. The cause of the prolonged hæmorrhage was the polypi, one of which had given rise to the carcinoma, probably fairly recently. It was very dangerous to attribute bowel hæmorrhage to diverticulosis or diverticulitis; it was usually due to carcinoma or polypi, which might be precarcinomatous. It was very difficult to diagnose a ring carcinoma which did not bleed from a localized area of diverticulitis, both pre-operatively and even at operation, especially as both might occur in bowel which was the seat of diverticulosis.

Inflammation of an Appendix Attached to a Left-Sided Caecum.

Dr. Rose's next patient was an eighteen-year-old female patient, who two and a half years previously had had an attack of acute appendicitis, characterized by pain commencing in the umbilicus and radiating to the right iliac fossa. Her doctor, though he used both a McBurney's and a mid-line incision, could not find the appendix. Fortunately, the attack subsided then, but further attacks occurred, so that she was referred for treatment during a pain-free interval. During the attacks she was always very tender in the right iliac fossa. X-ray examination after a barium enema then showed that the fluid first filled the colon on the right side of the abdomen. It then crossed the abdomen in the colon from right to left and descended to the caecum in the left iliac fossa. The appendix was not visualized. (The heart was in the normal position.) Operation showed that the primitive dorsal colic mesentery was still present and was very long. The caecum had fallen to the left with the ascending colon, and the descending colon had fallen to the right. The bowel could be put in any desired position, so long was the mesentery. The appendix was at first retrocaecal, but it was so long that it crossed the abdomen to the right pelvic brim. It was thick-walled and surrounded by adhesions, and its base was blocked by a fæcolith. The position of the appendix explained why an organ starting on the left side of the abdomen caused right-sided symptoms and signs.

Trauma to an Elbow Joint.

A male patient, aged sixty years, was then shown by Dr. Rose. The patient had fallen over on the tip of the right elbow, which became painful and stiff. When he was

examined, one week after the injury, there was effusion in the right elbow joint with much tenderness over the olecranon process. Examination of the left elbow, as a comparison, showed a hard movable boss of bone in the triceps tendon above the left olecranon process. There had never been any history of injury to this joint. X-ray examination was made of both joints. That of the right elbow showed what appeared to be a fractured osteophyte of the upper end of the right olecranon. That of the left elbow showed a large boss of bone in the triceps tendon separate from the olecranon with some osteophytes also there. Dr. Rose said that it was obvious that this bilateral condition was present before the accident affecting the right joint. The incident showed the value of comparing the alleged normal with the affected joint.

Avulsion Fracture of the Third (or Fourth) Lumbar Vertebral Body.

Dr. Rose showed a fifty-year-old male patient, who had been lifting a four hundredweight weight when he felt something "crack" on the right side of the lumbar part of his spine. This was followed by a stabbing pain made worse with extension of the right thigh. Examination of the patient a day later showed that the lumbar part of the spine was fixed and the patient was in obvious pain. There was great tenderness in the right loin. The pain prevented voluntary movement of the right hip. X-ray examination showed a fragment of bone lying beside and between the bodies of the third and fourth lumbar vertebræ towards their anterior aspect. The patient was treated conservatively in bed without plaster. It was three months before he regained full painless movement of the spine, and that was aided by the physiotherapists.

Dissecting Aortic Aneurysm.

Dr. Rose then showed a man, aged seventy-three years, who had been known to have a large aneurysm of the abdominal aorta for the previous three years. Apart from its increasing in size, this aneurysm had caused no symptoms until one week before admission to hospital, when the patient commenced to suffer lancinating pain in both lumbar regions. The pain radiated to the groins. On examination of the patient, a pulsatile swelling was palpable in the abdomen and considerable tenderness was present in both loins and in the epigastrium. An X-ray examination showed no appreciable abnormality, and no calcification in the aorta or great vessels. A provisional diagnosis was made of a leaking abdominal aneurysm. Aortography (with 70% "Diodone" solution) was performed. The results were a little equivocal, but showed the dye to be outside the aorta, even though blood under pressure flowed through the needle.

Lumbar Spine Lesion for Diagnosis.

Dr. Rose's next patient, when first examined in March, 1952, had been a strong, healthy athletic boy of fifteen years, whose height was six feet and whose weight was 12 stone five pounds. He was complaining of severe backache centering over the upper lumbar region of the spine, which was made worse by standing and eased by lying down. The pain had been intermittently present for one month. It had originally commenced as a mild ache, which could not be attributed to any specific cause. There were no previous illnesses, save for faucial diphtheria at the age of five years. Examination of the patient disclosed tenderness over the first and second lumbar vertebræ. Movement of the lumbar part of the spine was diminished because it accentuated the pain. X-ray examination showed reduction of the intervertebral space between the first and second lumbar bodies. The results of all other investigations, including a full blood count, blood sedimentation rate determination and chest X-ray examination, were normal. The Mantoux reaction was negative. Treatment was by rest in bed for one month and abstention from all sport for twelve months. Under those measures, the pain and stiffness disappeared within a month and had not reappeared since, so that examinations had since always shown a normal spine. Serial X-ray films taken from the first examination until the patient was last examined in March, 1954, still showed some diminution of the space. Dr. Rose said that the diagnosis was obviously that of a benign lesion which seemed to implicate the intervertebral disk rather than the bone. There was no evidence of Scheuermann's disease, with its wedging of the vertebral bodies, or of tuberculosis.

Posterior Dislocation of the Left Shoulder.

Dr. Rose's last patient, an adult male, had been involved in a motor-car accident, during which he sustained a posterior dislocation of the left shoulder. The diagnosis was well evident clinically in that the head of the humerus could be felt behind the glenoid cavity. X-ray films were shown, which were self-explanatory.

Regional Jejunitis with Massive Lymphoma.

DR. KEVIN J. FAGAN showed a woman, aged forty-five years, who had complained of attacks of "colitis" since the age of seven years. At the age of eighteen years a laparotomy had been performed at Belfast and the appendix removed. Since October, 1953, her attacks of diarrhœa and colicky, mid-abdominal pain had become more severe and more frequent. She began to vomit at the height of an attack, and weight loss of one stone occurred. On examination the patient was found to be extremely thin, weighing five stone thirteen pounds. The results of clinical examination were negative. At operation on March 17, 1954, a massive lymphoma of the upper jejunal mesentery was found; the glands had ulcerated, and a loop of jejunum was adherent to it. Over the course of six feet of the jejunum there were scattered areas of thickening of the jejunal wall with subserous "tubercles". The thickening of the jejunal wall was sufficient to produce chronic obstruction. The involved six feet of jejunum were resected. Convalescence was uneventful, and the patient was discharged from hospital on March 31, 1954. Dr. C. S. Graham gave the following report on the operation specimen:

> Macroscopic: This is a length of small intestine. In four or five areas the wall is thickened and in at least two of these the mucosa is roughened and reddened and possibly ulcerated. The second specimen is labelled "mesenteric gland" and this is an enlarged and pale firm lymph node.
>
> Microscopic: This is a regional ileitis (Crohn's disease). The inflammatory pattern in the sections from the intestine is not quite typical, but that in the lymph node is.

Pyloric Stenosis.

Dr. Fagan's second patient, a man, aged fifty-seven years, had been admitted to the Royal North Shore Hospital of Sydney on November 30, 1953, with a history of intermittent vomiting for eighteen months. The vomiting had been gradually getting worse until two weeks prior to admission. On November 16 the vomiting had become continuous in character, and the patient had been admitted to Lewisham Hospital. There the vomiting settled down until November 24, when a barium meal X-ray examination was made, which started the vomiting again. Vomiting continued until December 2. A barium meal X-ray examination on November 24 revealed the presence of pyloric stenosis. The patient had a previous history of a bleeding ulcer in 1944 and a ruptured ulcer in 1951. On examination of the patient the epigastrium was tender to pressure and a right inguinal hernia was present. The blood pressure was 95 millimetres of mercury, systolic, and 55 millimetres, diastolic. On December 2 a subtotal gastrectomy was performed by Dr. Fagan. The patient's condition improved rapidly until he developed a fever of 100° F. and a sharp pain in the right subcostal region anteriorly. This was thought to be a localized patch of peritonitis due to a leaking duodenal ulcer. Subsequently the patient's condition again rapidly improved, and he was transferred to Princess Juliana Hospital on January 16, 1954. It was noted that X-ray examination on November 20, 1953, had shown an active tuberculous lesion, and the result of sputum examination was positive for *Mycobacterium tuberculosis*. The patient's condition in that regard had steadily improved.

Arterio-Venous Aneurysm of the Right Femoral Vessels.

With DR. V. H. CUMBERLAND, Dr. Fagan showed a boy, aged thirteen years, who had been shot through the right groin with a 0·22 rifle eighteen months before admission to hospital. The "through and through" wounds had healed uneventfully, but ever since the injury he had had a limp and a feeling of stiffness in the right groin, and a buzzing feeling in the right groin. He was able to run about, but after a game of football he suffered such pain in the right lower limb that he had to remain in bed for a few days. Examination of the boy showed the right thigh to be one inch greater in circumference than the left. There was a wound of entrance in the lower part of the buttock and a wound of exit two inches below the mid-inguinal point. There were a palpable thrill and a loud continuous bruit in this area. Occlusion of the right femoral artery abolished the thrill and bruit, and lowered the pulse rate from 70 to 44 per minute; the blood pressure was altered from 120 millimetres of mercury, systolic, and 45 millimetres, diastolic, to 130 millimetres, systolic, and 75 millimetres, diastolic. At operation on July 17, 1953, Dr. Cumberland controlled the

right common iliac artery with a Pott's clamp, through an incision in the lower part of the abdomen, while the arteriovenous fistula was dissected. There was a fistula 0·5 centimetre in diameter directly connecting the artery and vein below the origin of the *profunda femoris* artery. This was treated by quadruple ligation and excision of the portions of the femoral vessels containing the fistulous communication. The circulation in the limb was not impaired, and the boy left hospital well on August 8, 1953.

Peptic Ulcer.

Finally Dr. Fagan showed two patients, one with a chronic gastric ulcer and one with a chronic duodenal ulcer.

A man, aged fifty-three years, was admitted to hospital four hours after a large hæmatemesis (he claimed to have vomited three pints of black coffee grounds material with frank blood clots). He had had a duodenal ulcer in 1932, from which he recovered on medical treatment. He had been well until four weeks before his present admission when he began to get vague symptoms of nausea, weakness and dry retching in the mornings. He had no pain. At 11 a.m. on December 25, 1953, he suddenly felt weak and sick and vomited three pints of blood clots and altered blood. On admission to hospital he was not distressed or exsanguinated, but twelve hours later he vomited several pints of blood-containing material, his blood pressure fell to 100 millimetres of mercury, systolic, and 60 millimetres, diastolic, and his pulse rate rose to 160 per minute. At operation a few hours later a large chronic gastric ulcer was found on the posterior wall of the stomach near the lesser curvature and in the middle third. A Bilroth I gastrectomy was performed. The ulcer was histologically benign. The patient left hospital on January 9, 1954, after an uneventful recovery. He had been free of symptoms since.

A man, aged thirty-seven years, had first developed symptoms of duodenal ulceration in 1939. Since then he had been in hospital every year for either a hæmorrhage or a perforation. He was admitted to the Royal North Shore Hospital of Sydney on January 31, 1954, stating that he had had melæna for three days associated with severe constant epigastric pain radiating to the right scapula and unrelieved by food or alkalis. At operation on February 2, 1954, a large chronic posterior duodenal ulcer was found. It was considered unsafe to remove the ulcer, and a posterior Pólya-Hofmeister type of gastrectomy was carried out, the duodenal stump being dealt with by Bancroft's method. His recovery was uneventful, and he was discharged from hospital on February 13, 1954. Subsequently he suffered from mild dumping, but put on weight, had no pain, and was extremely grateful for the relief from pain.

Duodenal Obstruction due to Gall-Stone.

DR. V. H. CUMBERLAND showed a married woman, aged seventy-four years, who had been admitted to the Royal North Shore Hospital of Sydney on July 4, 1953, complaining of colicky abdominal pain and the vomiting of large quantities of fluids for three weeks. She had not been constipated during this illness. She gave a long-standing history of fatty dyspepsia, flatulence and recurrent attacks of pain in the right upper part of the abdomen. Physical examination of the patient disclosed tenderness in the right hypochondrium. Bowel sounds were increased, but no other abnormality was discovered. X-ray examination (horizontal and vertical) showed no abnormality. Treatment was commenced with continuous suction and fluids were administered intravenously to combat the dehydration. On the following day her abdominal pain had increased, and laparotomy was performed. The small gut was collapsed from the ileo-caecal valve to the duodeno-jejunal flexure. The gall-bladder felt thickened, but no stones could be palpated. The root of the mesentery contained much fat, and although the duodenum was not visualized entirely, no abnormality could be detected on palpation. The abdomen was closed. For three days after operation her condition was much improved, vomiting and abdominal pain were absent, and gastric suction and intravenous fluid therapy were suspended. Pain and vomiting commenced on the fourth day after operation, necessitating a recommencement of suction and parenteral fluid therapy. On July 11, 1953, lipiodol, 10 millilitres, was administered by mouth, and X-ray examination of the abdomen showed blockage of the first part of the duodenum with dye passing into the gall-bladder. At laparotomy on the following day, performed through an upper abdominal incision, it was possible to milk a large gall-stone, one inch in diameter and one and a half inches in length, from the duodenum through the flexure into the proximal part of the jejunum. The stone was then removed by a longitudinal incision in the antemesenteric surface of the jejunum, which was sutured transversely. Her post-operative convalescence was uneventful. She was discharged from hospital on July 21, 1953.

Retroperitoneal Tumour.

Dr. Cumberland also showed a man, aged forty-five years, who had been perfectly well until August, 1947, when he noticed the passage of black stools, which apparently resulted in anæmia. He was thought on one occasion during this illness to be jaundiced. Barium meal X-ray examination showed no abnormality, but he was treated as probably suffering from a peptic ulcer. Between 1947 and 1951 he had occasional attacks of malaise. The attacks would commence with shivering; he would then feel hot and would sweat. In December, 1951, he had a further attack accompanied by soreness in the right upper part of the abdomen, and on this occasion a rounded lump, which moved on respiration and appeared to be attached to the liver, was discovered in the right hypochondrium. It was thought that his condition might be amœbic hepatitis, although he had never suffered from diarrhœa, and examination of the rectum and sigmoid colon, together with repeated examination of stools, revealed no abnormality. He was given a course of emetine, which resulted in a prompt improvement in his general condition, associated with return of his temperature to normal. There was no change in the character of the abdominal tumour. Between December, 1951, and June, 1953, he had increasingly frequent similar illnesses, and the periods of malaise were tending to increase in length. In June, 1953, he was again treated for amœbiasis and was given a full course of treatment; again he responded dramatically to the exhibition of emetine. He remained in his normal health until December, 1953, when he had a further similar illness, which resulted in his being "off work" for two months. The abdominal tumour had remained approximately the same size, and presented the same characteristics as at the time of its first discovery. On January 14, 1954, laparotomy was performed, and a large tumour measuring six inches in diameter was found in the posterior abdominal wall, appearing anatomically to be replacing the pancreas. The duodenum was stretched tightly over the tumour, which had a consistency varying from hard to fluctuant. A large bore needle was introduced into the substance of the tumour, but only blood was withdrawn. A biopsy was taken which showed organizing hæmatoma. Hæmostasis was achieved with considerable difficulty. The common bile duct, the portal vein and the superior mesenteric artery appeared to be incorporated within the substance of the tumour. No other abnormality was discovered on abdominal examination; the liver looked and felt perfectly normal. Barium meal and barium enema X-ray examinations showed displacement of the duodenum and hepatic flexure respectively. Excretion pyelography revealed no gross abnormality of either kidney, and lateral aortography illustrated the vascular nature of the tumour.

Erythroblastosis Fœtalis.

DR. CLAIR ISBISTER arranged a demonstration showing diagnostic methods, treatment, pathology and results of treatment of hæmolytic disease of the newborn. A chart showed the results of treatment during the past four years at the Royal North Shore Hospital of Sydney; 65 women with Rh agglutinins had been confined for 80 pregnancies. The results of this experience will be published in a separate article. A diagram and photograph together with the exchange transfusion apparatus showed the technique for exchange transfusion. Photographs showed the clinical appearance of subjects of *hydrops fœtalis* and the pathology of the liver. X-ray films were shown of the mother during pregnancy, indicating how the condition could be diagnosed before delivery. Microscopic sections of liver and blood films were shown under microscopes. Two patients who had received exchange transfusions were presented.

Hepatic Coma due to Calculous Obstruction.

The Unit of Clinical Investigation presented two patients who had been suffering from hepatic coma due to calculous obstruction and who were relieved by a two-stage operation.

A single woman, aged sixty-six years, was when admitted to hospital rather stuporose and confused. No very coherent history could be obtained, but it appeared that she had suffered a severe attack of upper abdominal pain some twelve months previously. It had lasted three or four days and gall-stones were diagnosed, but she had had no pain subsequently. Occasionally she noticed that her urine was dark, and a fortnight before admission to hospital she first noticed that she was jaundiced. Her appetite had been very poor. She had lost a considerable amount of weight over the last few months. No other symptoms of note could be elicited. She was a small, wasted, mentally dull and

incoherent woman, looking much older than her stated age and strikingly jaundiced. Her tongue was dry and brown. The abdomen moved evenly with respiration. The liver was easily palpable, firm, smooth and generally not tender. In view of her jaundice the abdomen was examined repeatedly, and at times she appeared to react to deep palpation in the gall-bladder region. Digital examination showed the rectum to be full of fæces. No other abnormality was noted. The fæces were dark on the examining finger, but no obvious blood was present. There were anæmia (the hæmoglobin value was nine grammes *per centum*) and neutrophilia (the total number of white blood cells was 17,700 per cubic millimetre, and 88% of these were neutrophile cells and band forms). Tests of the liver function and serum chemistry gave the following results: thymol turbidity, four units; serum bilirubin content, 6·8 milligrammes per 100 millilitres; serum protein content, nine grammes *per centum*; albumin-globulin ratio, 1:1; serum alkaline phosphatase content, 72·6 units; blood urea content, 33 milligrammes per 100 millilitres; serum sodium content, 135 milliequivalents per litre; serum potassium content, 5·5 milliequivalents per litre; serum chloride content, 94 milliequivalents per litre.

The patient's condition continued to deteriorate until she became comatose. She had a low-grade intermittent pyrexia, and in view of her leucocytosis and obstructive jaundice a biliary infection seemed likely. Since the hepatic coma was steadily deepening, emergency laparotomy was performed on July 9, 1953.

Extensive adhesions were found between the stomach, duodenum and gall-bladder. The lesser omentum was very thickened, and the gall-bladder was surrounded by dense inflammatory tissue and contained numerous large calculi. The common bile duct was grossly dilated and filled with large calculi. The gall-bladder was gangrenous. It was opened through its fundus and emptied of calculi. No bile escaped. The common duct was exposed and opened for removal of several large calculi when suddenly bile gushed up into the wound. Without further ado a tube was inserted to allow biliary drainage, and the abdomen was closed in layers. After operation the patient's condition improved dramatically. Within two or three days she was much more alert and by July 15 she was able to sit out of bed and was taking nourishment quite well. Bile was draining well from the choledochostomy tube. On July 23 drainage ceased; and when "Diadone" was injected up the tube and the area screened, the tube was found to have come out of the common duct. It was therefore removed. Meantime, the patient's condition was improving. She was gaining weight, and her jaundice appeared to be subsiding. She refused further surgical treatment and was about to leave hospital when on August 22 she developed upper abdominal pain and vomiting and her jaundice again became obvious. A second-stage operation was performed on August 24. Local inflammatory changes were much less. The gall-bladder could not be identified; it appeared to have been destroyed by the inflammatory process. The common bile duct was reexplored, and several large calculi were removed from its lower end. The duodenum was opened to ensure that the ampulla had been cleared of calculi. It was afterwards closed in layers, and a Foley's catheter was inserted into the common duct towards the liver. The gall-bladder site was drained and the abdomen closed in layers. Convalescence after this operation was satisfactory, and eventually on September 16 the tubes were removed. The patient stated at that stage that, though she dimly remembered coming to hospital, she had no recollection whatever of her first two weeks in the ward.

A man, aged seventy-one years, was admitted to hospital in hepatic coma on October 11, 1953. He was extremely drowsy, and history taking was difficult. It appeared that he had experienced severe pain in the upper part of the abdomen and chest about a month before admission, lasting for one or two hours. His appetite had been poor, and his urine and stools were very dark in colour. He was a thin, deeply jaundiced old man lying more or less stuporose and answering questions only hesitantly and vaguely. There was evidence of weight loss and dehydration. The heart was fibrillating, but there was no evidence of failure. He appeared to be tender on deep palpation in the epigastrium. Biochemical studies gave the following results: serum sodium content, 125 milliequivalents per litre; serum potassium content, 5·3 milliequivalents per litre; serum chloride content, 95 milliequivalents per litre; blood urea content, 65 milliequivalents per 100 millilitres; serum bicarbonate content, 30 milliequivalents per litre; serum bilirubin content, 25 milligrammes per 100 millilitres; serum alkaline phosphatase content, 24 units; thymol turbidity, four units. The patient's condition was deteriorating perceptibly; he was taking practically no nourishment, and he was becoming increasingly drowsy. No more precise diagnosis than "obstructive jaundice" had been made, but he was submitted to laparotomy on October 16, again with a view to relieving the obstruction as an emergency measure. There was a considerable amount of free fluid in the abdomen; both the gall-bladder and common bile duct were distended and surrounded by extensive inflammatory adhesions. A catheter was inserted into the common bile duct after a considerable amount of biliary mud had been sucked out. On the following day he was still comatose, but three days later he was already less drowsy. He gradually took increasing amounts of nourishment by mouth and a week after operation had recovered enough interest to ask for a cigarette. Before operation he had been in a state of pronounced sodium chloride deficit, but this was corrected by giving these electrolytes in an oil mixture. Some three weeks after the operation his caloric intake was consistently more than 2000 Calories daily, and bile was being run into his stomach with each meal. This involved the passage of an intragastric tube; but when it was discontinued for a few days, he asked to be given the bile again, as it so improved his appetite and well-being. By November 23 he was fit enough for his abdomen to be explored again. A single large stone was found in the lower end of the common bile duct and removed. The gall-bladder, thick-walled and full of calculi, was also removed. The liver was cirrhotic, and much ascitic fluid was present. Again a catheter was left in the common bile duct for twelve days, draining the bile externally. His convalescence was complicated by the development of gross ascites, which required frequent tapping, up to 126 ounces being drained off at a time. There was doubt as to the extent of the contribution being made to the ascites by his heart, which was still fibrillating. Two months after the second stage he had also developed considerable œdema of the scrotum and buttocks, and mersalyl therapy was instituted. Gradually his condition improved, and he was now free from ascites and œdema and was eating and feeling well. He also stated that he had no recollection whatever of his first two or three weeks in hospital.

Visceral Substitution.

The Unit of Clinical Investigation then presented two patients in whom visceral substitution had been effected.

Transverse Colon for Œsophagus.

A married woman, aged seventy years, was found to be suffering from carcinoma of the œsophagus. The growth was inoperable and was causing complete obstruction as shown radiologically. The transverse colon was separated and swung upwards on its vascular pedicle through the œsophageal hiatus. Its hepatic end was anastomosed to the side of the œsophagus above the growth, its splenic end to the upper part of the jejunum. The patient's ability to take food was much improved, but there had been recurring attacks of obstruction since, though she still survived eight months after operation. The case is being reported in detail elsewhere.

Substitution of Caecum and Ascending Colon for Bladder.

A man, aged seventy-one years, was admitted to hospital on June 18, 1953, with a very extensive carcinoma of the rectum invading the base of the bladder and causing retention of urine (prostatic obstruction was excluded). An operation for construction of an artificial bladder was performed. The ileum and upper end of the ascending colon were transected, and the continuity of the bowel was restored. The terminal part of the ileum was brought up through the abdominal wall after implantation of the ureters into the caecum, the upper end of the ascending colon being blind-ended. The case is being reported in detail elsewhere.

Upper Ureteric Obstruction.

DR. ALBAN GEE presented four patients with obstruction of the upper part of the ureter.

The first patient was a woman of forty-nine years, who had complained of pains in the left loin for eighteen months. These occurred intermittently in attacks of a throbbing nature, at times severe, with radiation to the groin. They lasted for two or three days. There were no urinary symptoms, and the urine was free of abnormality. An excretion urogram failed to show any dye from this kidney, though the right kidney was functioning well. A retrograde pyelogram revealed a dilated pelvis with a sharply cut-off margin, and a ballooning out of the calyces. There appeared to be little cortex present, and only a trace of colour was obtained from this kidney with the indigo carmine test at cystoscopy. These findings were confirmed at operation, and a nephrectomy was performed.

The next patient was a man of twenty-eight years, who had had pain in the left loin for two months, and had felt generally in poor health for the past year. There were no other symptoms, and no abnormality could be found on physical examination. An excretion urogram showed delayed excretion from both sides, more so on the left. There was considerable pelvic and calyceal dilatation on this side, with a narrowing at the uretero-pelvic junction. The left ureter was not seen. There was a small stone in the lowest calyx of the left kidney. On the right side there was also a good deal of hydronephrosis, and several stones were also present. The urine was not infected. At operation on the left kidney, an aberrant artery with accompanying veins to the lower pole was divided, and the stone removed. Cystoscopic examination one month later revealed a greeny-blue colour response to the indigo carmine test—a considerable improvement. At the same time a right ureterocele was treated with diathermy. Further examination of this side was postponed until the reaction had subsided.

Dr. Gee's third patient was a student, who had had right ureteric colic, and who had passed a calculus after ureteric dilatation. His excretion urogram revealed dilated calyces, and a slowly filling dilated pelvis, indicative of an upper rather than a lower ureteric block. The symptoms appeared to indicate the possibility of a stone low in the ureter, and at cystoscopy an obstruction to the passage of the Braasch bulb was felt just above the bladder. Retrograde pyelography was then performed, and this showed considerable pelvic dilatation, without much calyceal involvement. Operation confirmed this, and an aberrant vessel causing this dilatation was divided.

Dr. Gee's last patient in this group was a woman of sixty-one years, who had had some pain in the right loin, with hæmaturia. Previously, a stone had been removed from the right kidney, and also one from the right ureter. An excretion urogram showed numerous stones in the left kidney, but no dye excretion. The right kidney contained a stone the size of a threepenny piece, and there was considerable dilatation of the pelvis and calyces of the upper ureteric type. Her blood urea estimation gave a figure of 42 milligrammes per 100 millilitres; and although her symptoms were slight, it was felt that removal of her urinary obstruction would undoubtedly allow the kidney to carry on much longer. Prior to operation, the ureter was dilated, but no lower obstruction was found. At operation, the ureteropelvic junction was found to be densely bound down by fibrous adhesions—probably the result of the previous operation—and a pyelolysis was performed. The stone was easily obtained, and a nephropexy performed to permit better drainage of the lower pole. Convalescence was uneventful, and her general health improved considerably.

In discussing these patients, Dr. Gee remarked that mostly the patient who presented with this type of obstruction was a young adult or even younger person, but that often symptoms did not occur till later when the urine became infected. Recurrent pyelonephritic attacks should always be investigated by excretion urography, as also should attacks of renal type pain. In that way, many kidneys would be saved by simple relief of the obstruction, and others by the addition of a plastic operation. Nephrectomy relieved symptoms, but should not have to be performed.

Solitary Renal Cysts.

Dr. Gee then presented two patients, each of whom had been found to have a large solitary renal cyst.

The first patient was a man, aged seventy-two years, whose local doctor had discovered a tumour in the left loin after he had reported for an overhaul. His only symptoms were tiredness and lack of energy. Excretion urography showed a rounded mass six inches in diameter attached to the lower pole of the left kidney. The whole kidney was compressed upwards and the collecting system almost obliterated. A retrograde pyelogram gave a similar picture, and at operation the cyst was excised.

The second patient had found a lump in her left loin, but had no symptoms at all. Her mass was smooth, rounded and freely movable, and the diagnosis of cyst was confirmed by excretion and retrograde urography. In this case there was no alteration of the calyceal outlines. At operation the floor of the cyst was raised to show a definite granulomatous margin, so nephrectomy was carried out. The pathological report indicated that the mass was a granuloma.

In discussing these patients, Gee mentioned that although a cyst could usually be diagnosed from a newgrowth with reasonable certainty, yet malignant changes did sometimes occur and exploration should be carried out.

Polycystic Disease of the Kidneys.

Dr. Gee then presented a man of sixty-four years, who had been referred because of heavy hæmaturia and a palpable mass in the left loin. There was an indefinite fullness in the right hypochondrium also, which under anæsthesia proved to be an enlarged right kidney. Bilateral pyelography disclosed polycystic disease. As the patient's blood urea content was 228 milligrammes per 100 millilitres, and as his bleeding had ceased, no surgical treatment was advised.

However, in a second case, that of a female patient, aged thirty-seven years, when the blood urea content was 130 milligrammes per 100 millilitres, and symptoms of headache and loin pain had occurred, Rousing's operation was proposed to puncture the cysts. Both kidneys were readily palpable, and it was felt that some arrest of renal degeneration from cystic pressure might occur with the collapsing of the cysts. It was hoped to operate on both sides in turn.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

BEAUTIFYING MEASURES AMONG THE NATIVES.[1]

To return from this digression to my subject I have only farther to observe that the estimation of female beauty among the natives (the men at least) is in this country the same as in most others. Unsatisfied, however, with natural beauty, like the people of all other countries they strive by adscititious embellishments to heighten attraction and often with as little success. Hence the native savage of New South Wales pierces the septum of his nose, through which he runs a stick or a bone, and scarifies his body, the charms of which increase in proportion to the number and magnitude of seams by which it is distinguished. The operation is performed by making two longitudinal incisions with a sharpened shell and afterwards pinching up with the nails the intermediate space of skin and flesh which thereby becomes considerably elevated and forms a prominence as thick as a man's finger. No doubt but pain must be severely felt until the wound is healed. But the love of ornament defies weaker considerations and no English beau can bear more stoutly the extraction of his teeth to make room for a fresh set from a chimney sweeper; or a fair one suffer her tender ears to be perforated with more heroism than the grisly nymphs on the banks of Port Jackson submit their sable shoulders to the remorseless lancet. That these scarifications are intended solely to increase personal allurement I will not, however, positively affirm. Similar, perhaps to the cause of an excision of part of the little finger of the left hand in the women, and of a front tooth in the men;[2] or probably after all our conjectures, superstitious ceremonies, by which they hope either to avert evil, or to propagate good are intended.

[1] From "A Complete Account of the Settlement at Port Jackson", by Watkin Tench (1791). From the original in the Mitchell Library, Sydney.

[2] It is to be observed that neither of these ceremonies is universal but nearly so. Why there should exist exemptions I cannot resolve. The manner of executing them is as follows. The finger is taken off by means of a ligature (generally a sinew of a kangaroo) tied so tight as to stop the circulation of the blood, which induces mortification, and the part drops off. I remember to have seen Colbee's child, when about a month old, on whom this operation had just been performed by her mother. The little wretch seemed in pain and her hand was greatly swelled, But this was deemed too trifling a consideration to deserve regard in a case of such importance.

The tooth intended to be taken out is loosened by the gum being scarified on both sides by a sharp shell. The end of a stick is then applied to the tooth which is struck gently several times with a stone, until it becomes easily movable when the coup de grace is given by a smart stroke. Notwithstanding these precautions I have seen a considerable degree of swelling and inflammation follow the extraction. Imeerawanyee[3] I remember suffered severely. But he boasted the firmness and hardihood with which he had endured it. It is seldom performed on those who are under sixteen years old.

[3] This refers to a native who with a companion Benelong was taken to England by Governor Phillip. He died in London in May, 1794. On his tombstone in the East End his name is shown as Yemmerrawanyea.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 51, of August 19, 1954.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

The Short Service Commission granted to 3/40109 Captain A. O. Donald is extended until 23rd December, 1955.

Citizen Military Forces.

Northern Command: First Military District.

Royal Australian Army Medical Corps (Medical).—To be Captain (provisionally), 9th July, 1954: 1/61842 Kevin Thomas Hobbs.

Southern Command: Third Military District.

Royal Australian Army Medical Corps (Medical).—The provisional rank of 2/127019 Captain R. H. D. Bean is confirmed.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps: First Military District.

Major J. R. Hutcheon is retired, 28th May, 1954.

Royal Australian Army Medical Corps: Second Military District.

To be Honorary Captain, 31st May, 1954: Derek Berg.

The following officers are placed upon the Retired List (2nd Military District) with permission to retain their rank and wear the prescribed uniform, 24th June, 1954: Majors B. P. Anderson-Stuart and E. B. Jones, and Captain B. Avis.

The following officers are retired, 24th June, 1954: Lieutenant-Colonels A. W. Bye, O.B.E., M. S. S. Earlam, N. W. Francis, G. B. D. Hall, S. C. M. Hiatt, W. A. Hugh-Smith, W. L. Macdonald, K. B. Noad, H. M. Owen, J. W. Ralston, K. C. T. Rawle, E.D., and F. V. Twohig, Major (Honorary Lieutenant-Colonel) G. C. Halliday, Majors D. W. H. Arnott, J. M. Byrne, F. H. M. Callow, R. Dick, A. R. H. Duggan, C. W. England, A. P. Findlay, W. E. Fisher, H. P. Fitzsimmons, W. I. T. Hotten, B. R. Morey, C. M. McCarthy, J. F. McCulloch, G. V. Rudd, H. O. G. Selle, R. P. Shalala and A. R. Woodhill, Honorary Majors H. J. Ham and C. R. M. Laverty, Captains J. F. Boag, P. L. Charlton, J. H. Coles, R. F. Dilger, B. Fisher, D. Fogarty, D. A. S. Fraser, J. Gribben, G. U. Grogan, C. W. Harris, L. E. Jabour, R. H. Kaines, L. F. Mandelson, A. B. McIntosh, T. F. W. Power, D. M. Ross, A. S. B. Studdy and K. S. Wallace, Honorary Captains F. W. Buddee, B. R. V. Forbes, M. Hurst, C. J. M. King, F. L. Nicholl, N. V. Orr and L. O. Rutherford, and Lieutenants J. R. Henry, F. J. Macqueen, C. M. McArthur, A. E. Wilkinson and E. F. Wilson.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR OCTOBER.

Overseas Lecturers.

ON Monday, October 4, Dr. George Pack, chief of the gastric and mixed tumour service at the Memorial Hospital, New York, will visit Melbourne and give the following series of talks: 12.30 p.m., "Pelvic Exenterations", at the Women's Hospital; 4 p.m., "Melanoma", at the Peter MacCallum Clinic; 8.15 p.m., "Bilateral Radical Mastectomy", at the Medical Society Hall.

On Tuesday, October 12, Dr. Rodney Maingot, surgeon at the Royal Free Hospital, London, will lecture at 8.15 p.m.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 28, 1954.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Acute Rheumatism	6(4)	3(1)	2	..	1(1)	..	..	..	12
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	1	..	..	..	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	2(1)	1	..	..	..	..	..	..	3
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	6(5)	11(10)	1	..	..	..	..	1	19
Diphtheria	4(2)	..	6(1)	..	2(2)	1(1)	..	..	13
Dysentery (Bacillary)	..	3(2)	..	..	1(1)	..	..	..	4
Encephalitis	..	2(1)	..	..	..	..	..	1	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	1	..	..	..	..	..	..	1
Infective Hepatitis	39(17)	26(17)	..	..	2	..	..	9	76
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	1	..	..	..	..	..	1
Leptospirosis	1	1(1)	1	..	..	..	..	..	3
Malaria	..	2(1)	..	..	..	..	..	..	2
Meningococcal Infection	10(5)	5(2)	2	..	..	..	..	..	17
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1(1)	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	9(6)	1(1)	2(2)	2	..	..	..	15
Puerperal Fever	..	1	..	..	1	..	..	..	2
Rubella	..	14(10)	1(1)	..	14(10)	..	..	..	29
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	18(13)	26(20)	7(4)	10(7)	2	..	..	..	63
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1(1)	..	..	..	..	..	1
Trachoma	..	..	..	..	1803	..	..	..	1803
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	45(36)	32(21)	13(4)	10(5)	10(7)	5(2)	..	..	116
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	3	..	..	..	..	..	3
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from Northern Territory.

in the lecture hall of the Royal Australasian College of Surgeons, Spring Street, on a subject to be announced later. Dr. Maingot has been visiting the Royal Prince Alfred Hospital, Sydney, as the William McIlrath Guest Professor. He is particularly interested in gastric and gall-bladder surgery. On Friday, October 15, he will visit the Royal Melbourne Hospital clinico-pathological meeting at 1 p.m.

On Friday, October 15, Dr. John T. Ingram, dermatologist at the Royal Infirmary, Leeds, will lecture at 8.30 p.m. in the Medical Society Hall on "Dermatological Reflections on the Quick and the Dead".

Dr. J. G. Scadding, dean and director of teaching at the Institute of Diseases of the Chest, Brompton Hospital, London, will lecture in the Medical Society Hall at 8.15 p.m. on the following dates: Tuesday, October 19, "The Use and Abuse of Antibiotics in Respiratory Disease"; Thursday, October 21, "The Coughing Child". Dr. Scadding will also visit Saint Vincent's, the Royal Children's, Austin, Alfred, Royal Melbourne and Heidelberg Repatriation Hospitals and the Gresswell Sanatorium.

Country Courses.

Horsham.

On October 9 the following course will be held at Horsham: 3 p.m., Dr. J. McB. White, "Eye Emergencies in General Practice"; 4.30 p.m., Dr. R. S. Hooper, "Head Injuries"; 8 p.m., Dr. J. W. Johnstone, "Uterine Prolapse". The local secretary for this course is Dr. A. L. Bridge, Lister House, Horsham. Telephone: Horsham 103.

Bendigo.

On October 16 the following course will be held at Bendigo: 2.15 p.m., Dr. H. B. Kay, "Hypertension"; 3.15 p.m., Professor Lance Townsend, "Emergencies in Obstetrics"; 4.30 p.m., Dr. J. B. Curtis, "Head Injuries". Dr. A. J. Walters, 514 High Street, Golden Square, Bendigo, is the local secretary. Telephone: Bendigo 228.

Flinders Naval Depot.

On October 13, at 2.30 p.m., Dr. B. Keon-Cohen will conduct a demonstration on "The Hazards of Athletics" at Flinders Naval Depot by arrangement with the Royal Australian Navy.

Fees.

Fees for lectures at Horsham and Bendigo, and for the evening lectures by the visitors from overseas set out above, are payable to the Post-Graduate Committee at the rate of 15s. per lecture, but those who have paid an annual subscription to the Committee may attend without further charge. The address of the Committee is 394 Albert Street, East Melbourne.

Notice.

LAENNEC SOCIETY.

THE next clinical meeting of the Laennec Society will be held in the Stawell Hall, 145 Macquarie Street, Sydney, at 8.15 p.m. on Tuesday, September 28, 1954. The subject is "Sarcoidosis", and the address will be given by Dr. J. G. Scadding, dean and director of studies at the Institute of Diseases of the Chest, Brompton Hospital, and physician and senior lecturer in medicine at the Post-Graduate Medical School of London.

Medical Appointments.

Dr. J. L. Bignell has been appointed a member of the Opticians' Registration Board of Victoria.

Dr. A. J. Stubley and Dr. R. N. Gooch have been appointed medical officers in the Mental Hygiene Branch of the Department of Health of Victoria.

Dr. S. Sunderland has been appointed a member and deputy chairman of the Advisory Committee to the Mental Hygiene Authority of Victoria.

Dr. J. W. Rollison has been appointed a member and chairman of the Nurses Board of South Australia.

Dr. L. R. Mallen has been appointed a member of the Nurses Board of South Australia.

Dr. R. J. Killalea has been appointed registrar in anæsthesia at the Royal Adelaide Hospital.

Deaths.

THE following deaths have been announced:

BURNELL.—Glen Howard Burnell, on August 26, 1954, at Adelaide.

JUTTNER.—Frank James Alexander Juttner, on August 27, 1954, at Tanunda, South Australia.

GREENAWAY.—Thomas Sacheverell Greenaway, on August 27, 1954, at Armadale, Victoria.

Diary for the Month.

SEPT. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPT. 22.—Victorian Branch, B.M.A.: Branch Council Meeting.
SEPT. 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPT. 24.—Queensland Branch, B.M.A.: Council Meeting.
SEPT. 28.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 30.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

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